The New England
Journal of Medicine

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Volume 235 OCTOBER 10, 1946 Number 15

SCARLET FEVER

An Epidemiologic and Bacteriologic Study of Cases Occurring in a Small Community

A. Daniel Rubenstein, M.D.,* and George E. Foley†

BOSTON

THE serologic classification of the hemolytic streptococcus has often been applied to the study of more or less circumscribed outbreaks of scarlet fever and other streptococcal infections[1–4] and to the investigation of samples of endemic cases occurring during the so-called "streptococcus season" in a given community.[5–8] There are, however, relatively few reports in which all or nearly all the endemic cases of scarlet fever occurring in a community have been studied bacteriologically as well as epidemiologically.

Perhaps the most complete information on the scarlet fever occurring in individual communities during a stated period is contained in the report of Schwentker, Janney and Gordon,[9] who performed bacteriologic and epidemiologic studies on scarlet fever in several villages in Rumania.

Studies in schoolrooms[10] and in families[11] suggested the hypothesis that the variety of serologic types of hemolytic streptococci recovered from patients when scarlet fever is endemic may be composed of innumerable so-called "pure-type" outbreaks occurring in basic units of the population.[5–8] The sudden appearance of scarlet fever in a rural community that, except for a single case, had been free of this infection for a year was regarded as an excellent opportunity for further investigation of the transmission of this disease, the serologic classification of the hemolytic streptococci being utilized at the same time.

General Description

Ipswich, where the present studies were done, is a community with a population of 6611, situated on the northern coast of Massachusetts. Milk is supplied by several dealers, some of whom market raw milk. In 1945 the town had a total of 930 school children in attendance at four elementary schools (three public and one parochial) and one high school. A single local theater attracts children from several surrounding communities. Children are discouraged from attending the theater when contagious diseases are prevalent and school is in session, but there are no restrictions during vacation or recess periods.

During the interval between January 2 and May 24, 1945, a total of 94 cases of scarlet fever was reported from this community, in contrast to 1 case reported in 1944 and 15 cases reported in 1943. Cases were scattered throughout the community, with no correlation with any of the various milk routes. Interestingly enough, one of the early cases due to Type 1 hemolytic streptococci occurred in a milk dealer who distributed raw milk, and several subsequent cases due to the same serologic type of hemolytic streptococcus occurred among the consumers of his product. His milk, however, had been removed from sale. At this time, Type 1 cases were appearing among persons taking milk from several other local and outlying dealers. Without complete investigation the original situation could have been misleading.

The original purpose of this study was to isolate and classify the hemolytic streptococci from all the cases occurring in the community. For one reason or another, throat cultures could not be obtained in certain cases. Of those cultured, Group A hemolytic streptococci[12] were isolated from 71 or 76 per cent of all the cases occurring in the community. The serologic types of these strains were classified according to Griffith's[13] slide-agglutination technic. The incidence of the various types is summarized in Table 1. The distribution of types in this community is not unlike that previously reported from certain other Massachusetts communities in 1942–1943[8] and 1944.[14]

The onset of cases by ten-day periods according to serologic type is represented in Figure 1. Cases occurring in 1943 and 1944 are represented schematically. The curve presents two distinct peaks,

*District health officer, Massachusetts Department of Public Health and instructor in epidemiology, Harvard School of Public Health.

†Technical associate in epidemiology, Department of Preventive Medicine, Harvard Medical School, and Department of Epidemiology, Harvard School of Public Health.

each composed of cases due to several different serologic types.

Cases in Schoolrooms

The first case appeared on January 2 in a child who attended Grade 3 of School 1. Type 2 hemolytic streptococci were isolated from this case. Within the next nine days 7 additional cases due to Type 2 appeared among the children in the same schoolroom. Concurrently, on January 4 and 5, 2 cases due to Type 19 hemolytic streptococci developed, and on January 6, 2 cases due to Type 1 also appeared in this schoolroom. No cases were reported from this schoolroom after January 9.

Table 1. *Distribution of Serologic Types of Hemolytic Streptococci Isolated.*

Type of Streptococcus	No. of Cases	Percentage
2	25	35
1	22	31
19-24*	10	14
6	7	10
10	4	6
8	2	3
9	1	1
Total	71	

*Cross-agglutination with the serums used.

On January 10 cases began to appear in other grades of the same school and, later in the same month and throughout February, in other schools in the community. Scarlet fever remained prevalent in the other grades of this school and in other schools during the winter and spring months.

In contrast to the abrupt outbreak in Grade 3, School 1, cases in the other grades and schools were scattered; sometimes only 1 or 2 cases were reported from a grade or school. Unlike the schoolroom outbreaks previously reported[10] there was no striking correlation between serologic type and schoolroom; primary cases due to different types occurred in the same room, and each type produced secondary cases in the same and other schoolrooms, as well as in nonschool contacts (Table 2).

As would be expected, 71 cases (76 per cent) occurred in children of school or preschool age. The attack rates for scarlet fever in the various schools of the community varied from 0.1 to 16.8 per cent (Table 3). The rate for school children was 5.0 whereas that for preschool children was 3.7 per cent.

Of the 71 cases occurring in school and preschool children, only 38 (54 per cent) could be accounted for by direct case-to-case contact. These contacts, together with extraschool cases secondary to schoolroom cases, are shown in Figure 2.

Cases in Families

All cases reported during the period of the study occurred in 49 families. Sixteen families (33 per cent) accounted for 58 cases (64 per cent). The hemolytic streptococci causing scarlet fever in 14 of these 16 families were classified according to serologic type (Table 4).

As previously observed[11] the hemolytic streptococci recovered in the cases occurring in a given family were invariably of the same serologic type, indicating that the secondary cases were the result

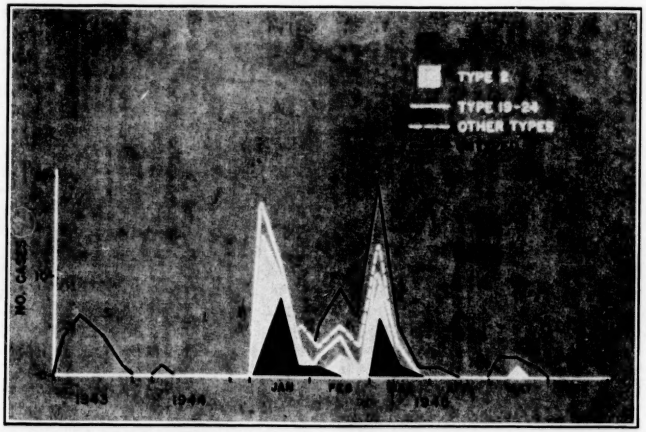

Figure 1. *Distribution of Cases of Scarlet Fever by Serologic Type.*

of household exposure. The intervals between the onset of the primary and secondary cases occurring in these families are shown in Table 5. It is noteworthy that more than a third of the secondary cases occurred more than twenty-one days after the primary case — the usual period of isolation for scarlet fever due to more than one type of hemolytic streptococci had occurred, multiple infections within a given family were due to a single serologic type. This correlation of type with family is in striking contrast with the lack of correlation of type with schoolroom shown in Table 2. Further-

TABLE 2. *Serologic Types of Hemolytic Streptococci Producing Scarlet Fever in Nonschool Contacts of Schoolroom Cases.*

CASES	TYPE OF STREPTOCOCCUS	WINSHIP SCHOOL GRADE							BURLEY SCHOOL	SHATTSWELL SCHOOL	FRENCH SCHOOL	HIGH SCHOOL	TOTAL
		1	2	3	4	5	6	TOTAL					
School primary	1			2				2					2
	2			1				1		1			2
	6								2				2
	8												
	9											1	1
	10									1			1
	19–24*											1	1
School secondary	1	3	1					4	1		1	1	7
	2	4	2†	7				11				1	11
	6												1
	8								1				1
	9												
	10												
	19–24*	1		2	2	1†	1	6		1		1	8
Totals		8	1	12	2	0	1	24	4	3	1	5	37
Nonschool secondary	1	4	4	5				13					13
	2	2		3				5		2			7
	6								2				2
	8												
	9												
	10									3			3
	19–24*											1	1
Totals		6	4	8				18	2	5		1	31‡

*Cross-agglutination with the serums used.
†Untyped cases in families in which other cases were all of this type.
‡Includes 5 Type-2 cases in a family with no school contact.

scarlet fever. According to our method of determining the interval between cases,* several secondary cases were as long as one hundred and thirty-two days removed from the primary case.

The role of the family in the spread of scarlet fever is further emphasized by the correlation of

TABLE 3. *Attack Rates of Scarlet Fever.*

CHILDREN	NO. OF STUDENTS	NO. OF CASES	ATTACK RATE %	
School children	1020	51		5.0
Winship	179	30	16.8	
Burley	184	7	4.2	
Shattswell	189	3	1.6	
French	90	1	0.1	
High school	378	10	2.6	
Preschool children	536	20	3.7	
Totals	1556	71		
Average				4.5

serologic types of hemolytic streptococci recovered from the primary and secondary cases occurring in a given family irrespective of the schoolroom attended by the patient with the primary case. In Table 6 school and nonschool secondary cases are divided according to family and school attended by the patient with the primary case and then arranged according to serologic type. Although 1 or more of the children in each family attended schools in which more, the appearance of cases due to a particular serologic type of hemolytic streptococci in a given schoolroom in many cases was shown to be the result of family spread from a child attending some other grade or school.

CASES WITH SOURCE ESTABLISHED

It has been reported that the hemolytic streptococci causing illness in a given group are usually of a serologic type not previously present in the population.[4] The heterogeneous type composition of endemic scarlet fever suggests multiple introductions of types previously not present in the community, in contrast to the introduction of a single type producing a well defined outbreak.[1] Whether the sudden increase from a single case in 1944 to 94 cases in the winter and spring of 1945 was due to a more or less general absence of hemolytic streptococci or of particular serologic types in 1944 followed by multiple introductions in 1945 cannot be stated definitely, since carrier rates were not studied. Two fairly clear-cut cases were established, however, in which scarlet fever was introduced into the community from outside sources.

One patient developed scarlet fever on the evening of the day he arrived home from California. Within the next two weeks, three family contacts (2 adults and 1 preschool child) and a next-door neighbor, who came to visit the patient, developed scarlet fever.

*In a theoretical family, Cases a, b and c occur. Time intervals *ab*, *ac* and *bc* are included in Table 5.

All cases were due to Type 2 hemolytic streptococci. The other child in the family who attended school was not ill, and was carrying Type 1 hemolytic streptococci in the throat. Although these cases were due to a type that had already appeared elsewhere in the community, in view of the data on multiple infections in families, there is little doubt

These cases, together with those occurring in schools and families for which a source of infection could be established, comprised 73 per cent of all cases occurring in the community (Table 7). If the 53 cases occurring as multiple infections in 14 families are omitted, however, only 16 (39 per cent) of the remaining cases can be accounted for by

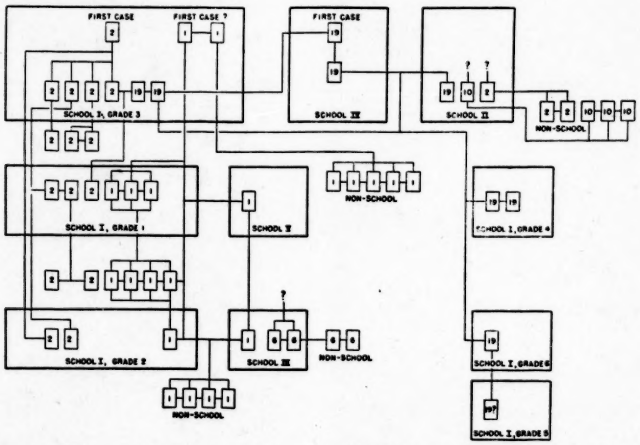

FIGURE 2. *Diagrammatic Representation of Spread of Scarlet Fever among School and Preschool Children.*

that the patient infected his family after he himself had been infected while en route home from California.

Another patient developed scarlet fever on the afternoon of the day he arrived home after several months' absence as a naval recruit. Type 8 hemolytic streptococci were isolated from nose and throat cultures. There was only 1 other case due to this

TABLE 4. *Serologic Types of Hemolytic Streptococci Isolated from Multiple Cases in Families.*

TYPE OF STREPTOCOCCUS	NO. OF FAMILIES	NO. OF CASES
2	7	22*
1	4	17
19-24†	1	6
10	1	4
6	1	4

*1 case not typed occurred in a family in which all other cases were Type 2.

†Cross-agglutination with the serums used.

type, which occurred in a young woman who lived across the hall from the patient. These infections developed late in the spring, near the end of the streptococcus season; otherwise it is conceivable that other cases might have originated from the patient.

recognized contact, even with fairly detailed bacteriologic and epidemiologic studies.

DISCUSSION

The role of the schoolroom[10, 15] and the family unit[14, 16] in the genesis of scarlet fever, as well as

TABLE 5. *Intervals between Multiple Cases in Families.*

INTERVAL *days*	NUMBER OF CASES	PERCENTAGE
0	7	7
1-7	27	28
8-14	19	20
15-21	7	7
22-132	36	38
Total	96	

in other infectious diseases,[17] is more or less established. The present study seems to be of particular interest in that, although the primary cases appear to have originated in the schoolroom, familial contact was the principal factor in maintaining the spread of the disease. Not only did a few families account for most of the cases occurring in the community but also the appearance of a case due to a given type in a schoolroom could sometimes

be accounted for by familial contact with a patient attending another schoolroom. The consistency with which a given type was recovered in all cases occurring in a family indicates that familial contact, rather than chance exposure to the same type of organism outside the home, was usually responsible for spread of infection. This was true not in-

comprising secondary waves were often caused by several serologic types. Since outbreaks of streptococcal infection usually result from the introduction of a type not previously present in the population, the sudden appearance of cases due to three different serologic types in this community suggests multiple introductions of new types

TABLE 6. *Correlation of Serologic Types of Hemolytic Streptococci Recovered from Primary and Secondary Cases in Families.*

FAMILY NO.	TOTAL PRIMARY AND SECONDARY CASES	PROBABLE SOURCE OF PRIMARY CASE	NUMBER OF CASES OF TYPE				
			1	2	6	10	19-24*
1	6	Winship (Grade 3)	6				
2	4	Winship (Grade 3)	4				
3	7	Winship (Grade 3)	7				
4	3	Winship (Grade 3)		3			
5	3	Winship (Grade 3)		3			
6	3	Winship (Grade 3)		3			
7	2	Winship (Grade 3)		2			
8	2	Winship (Grade 3)		2			
9	3	Shattswell		3			
10	4	Burley			4		
11	4	Shattswell				4	
12	4	High school					4
13	2	High school					2
14	6	?		6			
Totals	53		17	22	4	4	6

*Cross-agglutination with the serums used.

frequently in spite of the fact that the child who contracted scarlet fever attended a schoolroom in which cases due to other serologic types of hemolytic streptococci were occurring.

In several cases only a single case of scarlet fever appeared in a given schoolroom (Fig. 2). Since data on the Dick status of the children in these schoolrooms were lacking, it cannot be said that there were available susceptibles. As has been observed, however, the exhaustion of susceptibles is not the sole reason for the cessation of an outbreak of scarlet fever,[9, 10] and the lack of susceptibles is not the only explanation why an outbreak does not occur or continue to occur in a population unit infected with a suitable strain of hemolytic streptococci. The same phenomenon has been observed in studies of measles,[17] in which the introduction of a case into a population known to contain susceptibles did not give rise to secondary cases. The element of chance is perhaps a factor in such cases; for example, if the patient is exposed only to immune persons before being segregated, no new cases develop. In scarlet fever, furthermore, it is known that all susceptibles (as judged by the Dick test) who acquire the epidemic strain during the course of an outbreak do not develop clinical illness.[9, 10]

The data presented above differ from the studies by deWaal[15] and our previous experience with scarlet fever in schoolrooms[10] where the majority of cases in a given schoolroom was due to a single serologic type. Griffith[18] observed that although in schools the cases occurring in primary epidemic waves were usually due to a single type, the cases or else some unknown mechanism. Despite the multiplicity of human contacts complicating the epidemiology of scarlet fever, however, 2 cases were established in which the introduction of disease-producing streptococci into the community from outside sources was followed by secondary cases within the community.

Unlike Griffith's[18] studies the appearance of different serologic types as the cause of disease did

TABLE 7. *Cases with Known Source of Infection.*

SOURCE	NO. OF CASES
School contact	37
Extraschool familial contact	29
Extraschool nonfamilial contact	1
Extra-community contact	2
Total	69

not appear in distinct waves but occurred almost simultaneously (Fig. 1), the type composition of each of the peaks of high incidence being essentially the same. The type pattern in this community was not unlike that previously observed in different localities in Massachusetts,[6, 14] suggesting a fairly widespread distribution of the predominant types producing scarlet fever, and fluctuated only in relatively large units of time and space.

Although it is known that the ability to produce erythrogenic toxin is a characteristic easily acquired or lost,[5] there is no exact explanation why certain types suddenly appear in a community and attain predominance over other serologic types as a cause of streptococcal disease. Nor is the disappearance

of such a strain from the community clearly understood; for example, there is no adequate explanation for the absence of scarlet fever during 1944 in the community considered, although at the same time the type pattern producing disease in 1945 was present in other Massachusetts communities during 1943–1944.[5, 14] And there is no satisfactory explanation for the sudden appearance of 94 cases in this community in 1945, with type patterns similar to those previously observed elsewhere.

The succession of seasonal changes appears to be intimately related to the biology of the hemolytic streptococcus, or to its host-parasite relation. The times of high and low incidence of scarlet fever, for example, occur with surprising regularity over a period of several years.[14] Season seems to be a factor common to nearly all outbreaks of streptococcal disease, regardless of type composition, the majority occurring during the winter and early spring months. Griffith's[18] observation that the danger periods of school outbreaks in England are the Christmas and Lent terms applies equally to the observations made in this country. The heterogeneous type composition of endemic scarlet fever, with the parallel seasonal fluctuations in the prevalence of the predominant as well as the sporadic types recorded here and elsewhere,[14] suggests the operation of some factor other than serologic type in the spread of this disease.

Summary

Between January 2 and May 24, 1945, a total of 94 cases of scarlet fever occurred in a community with a population of 6611 as compared with 15 cases reported in 1943 and 1 case in 1944. The hemolytic streptococci isolated from 71 (76 per cent) of these cases were classified according to serologic type. Seven types were encountered: Types 2, 1, 19, 6, 10, 8 and 9 in order of frequency. The type pattern was similar to that previously observed in other Massachusetts communities during the period when the present community was experiencing little scarlet fever.

Seventy-one cases (76 per cent) occurred in children of school and preschool age. The first case appeared in Grade 3 of School 1 and was followed by a sharp outbreak of 11 additional cases in that room. Types 2, 1 and 19 appeared almost simultaneously in this schoolroom. Cases in other rooms of the same school were followed by the appearance of the disease in other schools in the community.

In the entire outbreak 49 families were involved. Of these, 14 contributed 53, or 64 per cent, of all the cases occurring in the community. In each case multiple infections in the same household were due to the same serologic type. Familial contact accounted for the appearance of sporadic cases in various schools other than those in which the primary cases originated.

There was no correlation between serologic type and schoolroom attended, but there was a correlation between serologic type and family. This suggests that although infection was introduced into the family from the schoolroom, familial contact was the principal factor in maintaining spread.

Other than multiple infections in the same household, a source of infection could be established with the help of serologic classification in only 16 (39 per cent) of the remaining cases.

We acknowledge the assistance of Dr. Robert E. Archibald, district health officer, Massachusetts Department of Public Health; Dr. Frank Collins, chairman, Board of Health, Ipswich; Mr. Paul Jodoin, agent, Board of Health, Ipswich; and Mrs. Jerome Meyer, R.N., School Department, Ipswich.

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ACUTE SALPINGITIS DUE TO *FRIEDLÄNDER'S BACILLUS*

Report of a Case

THOMAS W. BOTSFORD, M.D.,* AND THOMAS D. KINNEY, M.D.†

BOSTON

IT is the purpose of this paper to report a case of acute salpingitis in an eighty-year-old woman, caused by *Klebsiella pneumoniae*. Acute suppuration of the fallopian tube in elderly women is rare, and salpingitis due to this organism is doubly unusual. Extrapulmonary *K. pneumoniae* infections have received increasing attention in published reports during the last few years. In 1937 Baehr, Shwartzman and Greenspan,[1] reporting a study of 198 cases found only 6 (3.5 per cent) with infection in the vagina, uterus or adnexa. Other cases of Friedländer-bacillus infections of the female genital tract have been reported by Scheyer,[2, 3] Reichert[4] and Hepp.[5]

CASE REPORT

Mrs. B. H., an 80-year-old widow, entered the Surgical Service of the Peter Bent Brigham Hospital on October 21, 1945, complaining of lower abdominal pain of 6 hours' duration. In 1938 a diagnosis of diverticulosis had been made on barium-enema studies by the family physician. About 6 hours before entry, while riding in a car, the patient experienced a sudden pain just below the umbilicus that quickly shifted to both lower quadrants. The pain was severer on the left than on the right side and was steady in character but was not severe enough to double her up. She was nauseated but did not vomit. She had had a normal bowel movement shortly before the onset of the pain. There had been no changes in bowel habits, and she had noticed no blood or pus in the stools. The bowels had moved once daily with the occasional use of milk of magnesia.

The past history revealed that the patient had undergone a cholecystectomy in 1934 for cholelithiasis. In 1941 she was treated on the Medical Service of the Peter Bent Brigham Hospital for unresolved lobar pneumonia of the right upper lobe. She had subsequently been followed carefully by the family physician, who had examined her sputum on numerous occasions and had found no tubercle bacilli. She had never had hemoptysis and brought up little sputum. In December, 1942, a check-up chest film was reported to show dense fibrous tissue in the right upper lobe with a cavity. Findings were thought to be compatible with an organizing Friedländer-bacillus pneumonia with residual cavity. No Friedländer's bacilli had ever been isolated from the sputum.

There was no family history of typhoid fever, diabetes, tuberculosis, cancer or blood diseases.

Physical examination showed a thin woman lying in bed in no apparent distress. The rectal temperature was 99°F., the pulse 84, and the respirations 26. The blood pressure was 132/82. The chest was clear except for diminished breath sounds over the right upper lobe. The heart was not enlarged, and the sounds were regular and of good quality. The peripheral arteries were firm and tortuous on palpation. The abdomen was moderately distended, and peristalsis was diminished. There was tenderness over the entire lower abdomen but more marked in the left lower quadrant. Involuntary muscular spasm was present in the left lower quadrant, and rebound tenderness was referred. No masses were palpable. Rectal and pelvic examination showed tenderness on the left, but no masses were palpable. The uterus was small, and there was no pain on movement of the cervix.

Examination of the blood showed a hemoglobin of 12.0 gm. and a white-cell count of 17,600. The blood smear showed 78 per cent neutrophils, 18 per cent lymphocytes and 4 per cent monocytes. Urinalysis was not remarkable. The blood urea nitrogen was 9 mg., and the plasma protein 6.5 gm. per 100 cc.; the chloride was 85 milliequiv. per liter.

The provisional clinical diagnoses were diverticulitis, with pelvic peritonitis, unresolved pneumonia of the right upper lobe and arteriosclerosis of the peripheral arteries.

The patient was observed for 8 hours, during which a plain film of the abdomen and a chest film were made. The former was essentially negative, and the latter showed extensive pulmonary fibrosis with a cavity in the right upper lobe similar to that reported in the chest film made in 1942. A

FIGURE 1. *Low-Power Photomicrograph of Fallopian Tube. Note the diffuseness of the inflammatory reaction.*

Miller–Abbott tube was passed because of the diminished peristalsis and abdominal distention. At the end of the period of observation the tenderness and spasm in the left lower quadrant had increased, and the temperature had risen to 101.2°F. by rectum. The white-cell count rose to 23,000. Because of these changes operation was carried out about 8 hours after entry.

Laparotomy under ether anesthesia was performed through a left-lower-quadrant, rectus-muscle-splitting incision. A moderate amount of thick exudate was present in the pelvis,

*Instructor in surgery, Harvard Medical School; formerly, resident in surgery, Peter Bent Brigham Hospital.

†Instructor in pathology, Harvard Medical School; associate pathologist Peter Bent Brigham Hospital.

and the sigmoid showed numerous diverticulums covered by thick plaques of fibrin. The left fallopian tube overlay the lower sigmoid, and its distal two thirds was markedly swollen and inflamed. The fimbriated end of the tube was attached to the sigmoid, and when it was freed, thick yellow pus escaped. A left salpingectomy and sigmoidostomy were performed, and the wound was closed around the loop of sigmoid without drainage. Cultures of the pelvic exudate and pus from the fallopian tube grew a Type A Friedländer's bacillus. The postoperative diagnoses were acute salpingitis of the left fallopian tube, acute diverticulitis of the sigmoid and pelvic peritonitis.

After operation the course was uneventful. The Miller–Abbott tube was removed on the 3rd postoperative day. The patient was afebrile by the 5th postoperative day. She received 4 gm. of sulfadiazine daily, a blood level between 10 and 15 mg. per 100 cc. being reached. This was discontinued on the 16th postoperative day. The patient was discharged

FIGURE 2. *High-Power Photomicrograph of Fallopian Tube. This shows the nature of exudate in the lumen of the tube.*

on the 20th postoperative day, when the colostomy was functioning well and she was asymptomatic. A check-up 2½ months later showed her to be still doing well. A culture of the colostomy at that time grew no Friedländer's bacilli, but she had developed a small abscess in the operative wound, which was drained. A Type A Friedländer's bacillus was recovered from the culture. The organism was also isolated from the sputum for the first time.

The left fallopian tube measured 7 cm. in length. The diameter of the tube varied from 0.7 to 1.9 cm. The distal two thirds of the tube was swollen and tense, and its serosal surface was dark red and covered by many patches of waxlike fibrinous exudate. The fimbriated portion was ragged and inflamed and covered by exudate. The muscular layers of the tube were swollen. The lumen was patent and was distended by the presence of a large quantity of soft, thick, yellow-white exudate. The mucosa was dull red and ulcerated in places. Microscopic sections showed the muscular, mucosal and serosal layers of the tube to be diffusely infiltrated by polymorphonuclear leukocytes (Fig. 1). The lumen of the tube was distended by exudate made up, for the greater part, of polymorphonuclear leukocytes and containing large numbers of bacteria (Fig. 2). Stains showed these bacteria to be encapsulated, short, gram-negative bacilli.

The fact that Type A strains of Friedländer's bacillus were cultured from the sputum, the pelvic cavity and the fallopian tube is suggestive evidence that the lungs were the portal of entry for the organism in this case. Julianelle,[6] in a study of eighty strains of *K. pneumoniae* gathered from various sources found that 52 per cent were Type A, 15 per cent Type B, 9 per cent Type C and 24 per cent Group X. It is of interest to note that 70 per cent of the Type A strains were associated with pneumonia in human beings. Similarly Perlman and Bullowa[7] and Solomon[8] reported series of cases of Friedländer-bacillus pneumonia in which the Type A strains were the infecting organisms in the great majority. Recently Kinney and Ginsberg[9] stressed the significance of serologic typing of Friedländer's bacillus, and reported 7 cases of liver abscess in which all the organisms except one belonged to other groups than Type A. They further pointed out that Type A, in their experience, was usually associated with respiratory infections. These studies add supportive evidence to the thesis that the patient first suffered from a Friedländer-bacillus pneumonia, and that the tubal infection was metastatic from the lungs.

The sulfonamides have been used in the treatment of *K. pneumoniae* infections with varying results. Heilman[10] reported the use of streptomycin in experimental infections, with encouraging results. Herrell and Nichols[11] have stated that they successfully used streptomycin in 45 patients. The patient reported above was treated with sulfadiazine, but the pulmonary infection was unaffected. It must be emphasized that localized infections should be treated surgically in the same fashion as any pyogenic infection. The patient responded well to salpingectomy and drainage of a wound abscess, both associated with a Type A Friedländer's bacillus. She was not given streptomycin, but Herrell and Nichols[11] mentioned 4 cases of ozena due to Friedländer's bacillus in which the symptoms were relieved by intramuscular streptomycin in total dosage of 9,600,000 to 14,000,000 units over a period of several days.

SUMMARY

A case of acute salpingitis due to Friedländer's bacillus occurring in an eighty-year-old woman is reported. The patient was treated by salpingectomy with recovery. A Type A Friedländer's bacillus was recovered from the sputum, peritoneal cavity, fallopian tube and a postoperative wound abscess. It is suggested that the lungs were the primary focus of infection. The literature is briefly reviewed.

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THE CAUSE, RELIEF AND PREVENTION OF HEADACHES ARISING FROM CONTACT WITH DYNAMITE

First Lieutenant Arthur M. Schwartz, M.C., A.U.S.

As early as 1910 Laws[1] described the so-called "Nitroglycerin head," and several papers soon followed that helped to elucidate the physiologic effects of nitroglycerin on the human body, especially after the absorption of extremely minute quantities through the unbroken skin, or even the inhalation of the fumes when dynamite is used for blasting purposes.[2–4]

Men working in powder plants soon acquire a rather transient immunity to nitroglycerin that can rapidly be lost over a period such as a weekend or during a vacation. Return to the job consequently results in a severe headache, which is also experienced by men first starting to work with dynamite. Such men subsequently discover that the application of a small amount of dynamite within the sweatbands of their hats provides a sufficient immunity to lessen the likelihood of a headache after prolonged contact with dynamite. The headache and its associated symptoms are so severe that it is not unusual for the men to be somewhat irritable, pugnacious and difficult to get along with. A case of homicide has been reported in which a man experiencing a severe dynamite headache drank an alcoholic beverage, which increased the dilatation of the intracerebral vessels and greatly magnified the headache. A display of maniacal manifestations is not unusual.[5, 6]

With the advent of war it was necessary for many large groups to be exposed to the handling of dynamite and other demolition agents, particularly "C_2." The following report is based on a study conducted at a Pacific combat training center, where considerable quantities of dynamite were dealt with daily to simulate battle conditions and adequately to prepare troops for engagement with the enemy.

Primary interest was in a group of 10 men whose principal duty involved intimate contact with dynamite (20 per cent nitroglycerin), and whose subsequent complaints were intense throbbing headache, nausea, some vomiting and occasional tremors of the upper extremities. Between 8:00 and 11:00 a.m. each man was required to handle several hundred sticks of dynamite. At noon on the same day the 10 men frequently reported to the post dispensary because of intense, severe, debilitating headaches; they wanted something to relieve the throbbing, the tenseness of the scalp, the nausea and the sensation that the top of the head was "ready to blow off."

The problem was approached on the basis of the following considerations: the cause of the headache; the degree of psychogenic element present in its development; possible drugs or combinations of drugs to reduce the severity of the headache once initiated; and prophylaxis to eliminate or diminish the occurrence of the headache.

It is interesting that these men actually dealt with two distinct types of explosives: C_2, a substance closely allied to trinitrotoluol with an oily base, which is molded to fit around such a structure as a pillbox and must be detonated with some form of cap; and dynamite, which contains 20 per cent nitroglycerin and can be exploded by dropping from a suitable height or striking with a heavy object. All men, at one time or another, had witnessed a serious accident from a dynamite explosion involving loss of limb or life — the possible psychogenic factor is obvious. Some form of controlled experiment was required to prove the identity of the offending substance. Patch tests in which dynamite was used and similar ones employing C_2 were prepared. The patch, which contained enough dynamite to cover the surface of a dime, was applied to the back over the left scapula of 15 men reporting for morning sick call; these men, who were told nothing of the nature of the substance applied to their backs, had complained of symptoms in distant, unrelated portions of the body. Fourteen subjects returned three hours later complaining of severe throbbing headaches, associated with a feeling of warmth over the face, and some nausea, and 1 reported the appearance of scintillating bodies in the right visual field. These men were given two aspirin tablets with no relief. In several cases the severity of the symptoms was increased. None of the 15 subjects tested with C_2

complained of headache after the passing of an equal period.

What are the mechanisms and the physiologic processes involved in a nitroglycerin headache? Ten subjects who handled dynamite were skin tested with an intradermal injection of 0.01 mg. of histamine (0.01 cc. of a 1:1000 solution); approximately 90 per cent developed a marked cutaneous reaction, with pseudopodia and much erythema. In fact, this minute quantity was sufficient in one subject to reproduce the headache described under the influence of dynamite. Goodman and Gilman[7] state that nitroglycerin and nitrites produce an increase in intracranial pressure that is principally due to cerebral vasodilatation, but do not make clear whether the intracerebral or extracerebral vessels are involved. Schumacher and Wolff,[8] differentiated headaches arising from dilatation of the arteries of the scalp and dura and those due to dilatation of the intracerebral vessels. The histamine headache, which is included in the latter group, is relieved by an increase in the cerebrospinal-fluid pressure effected either by pressor drugs or by direct raising of the pressure. In contrast, the headache that is present in migraine and hypertension and is produced by dilatation of the vessels of the scalp and dura is not affected by an increase in the cerebrospinal-fluid pressure, which merely increases the difficulties when one considers the action of nitroglycerin on the cerebral vessels.

From all available sources and from personal observation it appears that the headache produced by contact with nitroglycerin is closely analogous to that caused by histamine injection. Examination of the fundi at the height of the headache tends to support this claim. The retinal vessels — especially the arteries — of all subjects reveal marked dilatation. With histamine injection a similar vasodilatation of intraocular vessels is observed. All but 1 of the 10 subjects displayed a substantial hypotension, the systolic blood pressure varying between 85 and 110 at the time of the dynamite headache; the normal average systolic pressure for this same group was 119. This lowered arterial pressure is associated with a proportionately reduced spinal-fluid pressure.[9] Relief of the headache requires a drug with vasoconstricting and pressor effects, which subsequently tends to elevate the cerebrospinal-fluid pressure.

Gottlieb[10] was principally concerned with the vasoconstricting and concomitant pressor action of amphetamine (Benzedrine) sulfate in migraine attacks. In addition, this drug reduces the amplitude of the pulsations of the cranial arteries. As in the migraine syndrome, the headache of nitroglycerin causes extreme fatigue and mental slowness. In many cases adequate performance of simple daily tasks is impossible. Gottlieb administered amphetamine sulfate intravenously and aborted the migraine attack but considered small repeated doses necessary to prevent a recurrence.

A series was set up in which 10 subjects who had never handled dynamite were given amphetamine sulfate orally, 5 mg. in the early morning and 10 mg. at noon. This schedule was carried out three days before the initial contact with dynamite. The subjects were subsequently given the patch test with dynamite described above. None of the group complained of headache after three hours of continuous exposure to 20 per cent nitroglycerin. Some of the usual side actions of amphetamine were noted, including difficulty in falling asleep and a moderate amount of nervousness.

Pelner and Aibel[11] obtained gratifying results in 60 patients with periodic and histamine headaches who were given gradually increasing doses of prostigmine bromide orally. Acetylcholine was believed to be a factor in the headache, and desensitization with oral prostigmine bromide was considered possible. The 10 subjects in the series who continuously dealt with dynamite had a common denominator, namely, a marked local cutaneous reaction to intradermal histamine injection. Histamine is a substance with physiologic properties similar to those of acetylcholine. Intradermal injection of either drug produces dilatation of cerebral vessels. Prostigmine, which is an inhibitor of cholinesterase and can mobilize the acetyl choline reserves of the body, lessens the reaction when histamine is released outside tissue cells. One might speculate whether histamine is released in persons in contact with nitroglycerin.

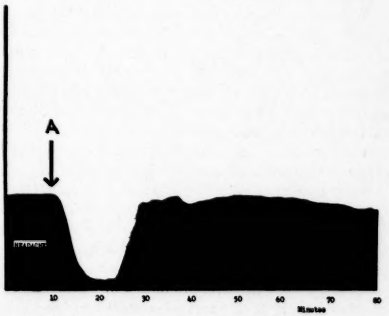

FIGURE 1. *The Effect of Adrenalin.*

This graph represents the effect of the injection of 0.5 cc. of a 1:1000 adrenalin solution (A) *on the average subject with a nitroglycerin headache. The patient experiences immediate relief from the severe headache, but within the passing of a few minutes the symptoms return and in many cases are more pronounced than before the injection.*

The purpose was to expose the subjects to gradually increasing doses of prostigmine bromide. Forty-five milligrams of the drug was dissolved in 60 cc. of water, and the men were instructed to take one drop

in the morning, two at noon and three at night on the first day. An increase of one drop for each dose was ordered until thirty drops had been taken, when thirty drops daily for an entire week, and subsequently thirty drops three times a week, were taken. When the men were receiving thirty drops three times weekly, they were asked to handle dynamite continuously for a full day without the usual precautions, that is, rubber gloves. During the time when they were taking prostigmine bromide the men were not in contact with dynamite. This was necessary to ensure against any transient immunity that might be developed from contact with dynamite. At the completion of a full day's work with dynamite only 20 per cent of the group complained of headache, and this was of a nature that did not require medication for relief.

Early in the study a method of obtaining immediate relief for these men whose assignment brought them in continuous daily contact with dynamite

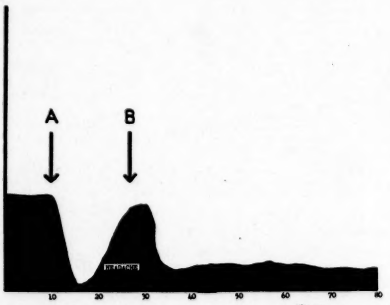

FIGURE 2. *The Effect of Ergotamine Tartrate.*

This graph represents the immediate and later effects of two injections of 0.25 mg. of ergotamine tartrate (A *and* B), *spaced seventeen minutes apart, on the average subject with a nitroglycerin headache.*

was sought. A drug with marked vasoconstricting and pressor effects, such as adrenalin, caffeine sodium benzoate, ergotrate, amphetamine sulfate or ergotamine tartrate, appeared to be required. Such analgesics as aspirin, phenacetin, codeine and the barbiturates were without beneficial effect and in many cases increased the severity of the headache and other symptoms. Adrenalin, in a dose of 0.5 cc. of a 1:1000 solution, produced transitory relief lasting only several minutes and was soon followed by an increase in the symptoms, possibly owing to the vasodilating effect following vasoconstriction (Fig. 1). Ergotrate, in a dosage of 0.2 mg., likewise produced only a momentary obliteration of the headache. After receiving the ergotrate several subjects experienced increased nausea and abdominal cramps — a frequent side action of ergotrate. Ergotamine tartrate,[12] in a dosage of 0.25 mg. subcutaneously was given and produced lasting relief in about 40 per cent of the subjects and a transient effect in 60 per cent (Fig. 2). The greatest relief for the headache caused by contact with nitroglycerin was obtained with an intramuscular injection of 0.5 gm. of caffeine sodium benzoate, followed by 5 to 10 mg. of amphetamine sulfate orally (Fig. 3). The systolic blood pressure and the cerebrospinal-fluid pressure rose after a subcutaneous injection of amphetamine sulfate. This is significant because in a nitroglycerin headache there is a reduced arterial pressure and subsequently a reduced spinal-fluid pressure.

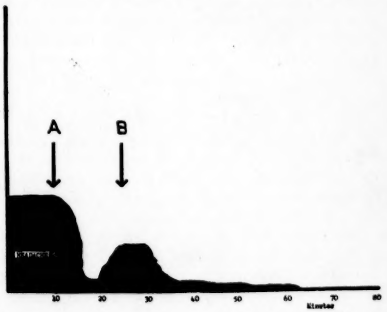

FIGURE 3. *The Effect of Caffeine Sodium Benzoate followed by Amphetamine Sulfate.*

This graph represents the effect of the intramuscular injection of 0.5 gm. of caffeine sodium benzoate (A), *followed in fifteen minutes by the oral ingestion of 5 to 10 mg. of amphetamine sulfate* (B), *on the average subject with a nitroglycerin headache. This combination gave the best results.*

sure. About an hour after the ingestion of 10 mg. of this drug a moderate rise in the systolic blood pressure, with marked relief of the headache, was observed.

Several laboratory procedures were performed, to give some indication of the physiologic effects of dynamite at the time of the headache. The results of routine blood counts and smears in all subjects were within normal limits. Urine analysis at the height of the headache revealed no glycosuria in any case, in spite of the fact that it has been reported that transient glycosuria occurs in such cases.[3] Electrocardiograms were taken at the time of the headache, and in all cases essentially normal tracings were obtained. It was decided to determine accurately whether or not oral prostigmine bromide was desensitizing these men to histamine. The same subjects — those who had marked cutaneous reactions to histamine, as well as those who had been ingesting prostigmine — were given additional skin tests with 0.01 mg. of histamine solution. In 90 per cent the severity of the local reaction was markedly reduced. Before oral desensitization with prostigmine bromide, the average

diameter of the wheal produced was 1.3 cm.; after desensitization the average diameter was 0.45 cm., a significant reduction.

Summary

The prime factor in the production of headache following contact with dynamite is its 20 per cent content of nitroglycerin, which can be absorbed through the unbroken skin to produce marked symptoms directly related to vasodilatation of the intracerebral vessels.

The psychogenic factor of fear did not play a role in the activation of the headache in subjects who were unaware of the nature of the patch test. It is entirely possible that some psychic element is active in subjects who realize the dangers associated with dynamite handling, but such a factor is not considered significant.

The intramuscular injection of 0.5 gm. of caffeine sodium benzoate followed by oral administration of 5 to 10 mg. of amphetamine sulfate greatly reduced and alleviated the symptoms of headache and within an hour gave lasting relief in over 95 per cent of the subjects.

The administration of 15 mg. of amphetamine sulfate daily for two or three days before exposure completely prevented the occurrence of the headache in all subjects, with minimal side effects.

Daily administration of oral prostigmine bromide in gradually increasing doses protected approximately 80 per cent of the subjects from the symptoms caused by nitroglycerin contact. It is quite reasonable to assume that desensitization results from a gradual liberation of minute quantities of acetylcholine that shock the intracerebral vessels to dilatation at regular intervals.

570 West 204th Street
New York City

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TERMINAL ILEITIS WITH OBSTRUCTION AND ABSCESS COMPLICATING PREGNANCY

William W. Babson, M.D.*

Gloucester, Massachusetts

IT IS the purpose of this paper to report and discuss a patient with cicatrizing ileitis, accompanied by obstruction and abscess, who was observed during the seventh month of pregnancy.

Regional ileitis is the most frequent chronic inflammatory disease of the small bowel and its mesentery. After Crohn[1] directed attention to this disease in 1932, sufficient operative cases had been reported by 1939 to allow Shapiro[2] to tabulate 519. Its occurrence in a severe form during pregnancy, however, has not been reported in the literature. Intestinal obstruction is also an unusual complication of pregnancy. Hansen,[3] in 1941, noted 84 cases recorded in English. Williams[4] mentions 2 cases in 30,000 deliveries. Slemons and Williams,[5] in an analysis of types of intestinal obstruction recorded in the world literature, did not mention ileitis as a cause.

Surgical complications — particularly obstruction — in pregnancy should always be considered by the family physician, obstetrician and surgeon; the difficulty of recognizing such complications is well known. Pain is nearly always the prominent symptom. Blakely[6] stated that the source of pain in pregnancy can be determined if a little care is taken in questioning and investigating the patient. Although pain frequently occurs in pregnancy, it should never be considered lightly, for it is occasionally the result of a serious pathologic state.

The management of acute surgical complications in pregnancy often presents a problem. Authorities are quite well agreed on certain aspects; on others, individual judgment is necessary, and no single rule can be laid down.

It is believed that these facts make the following case worthy of note.

*Surgeon, Addison Gilbert Hospital.

Case Report

A 25-year-old primipara was admitted to an Army Air Forces regional hospital on April 12, 1945, because of abdominal pain and vomiting during the 7th month of pregnancy. Two months previously the patient had had an episode of diarrhea, vomiting and fever, for which she had been admitted to the obstetric service of this hospital. The symptoms subsided, and she was discharged after 3 hospital days, with a diagnosis of gastroenteritis. On the next evening she had a sudden, severe pain in the right lower quadrant that was steady and nonradiating and gradually decreased in severity. There was local tenderness and discomfort on motion and deep breathing. On the following day a physician stated that the pain was the result of pressure. The patient had subsequently had recurrent, shifting, sharp pain over the entire abdomen, gas pains and often steady pain in the right lower quadrant. The shifting pains were relieved by the passage of flatus or by bowel movements. The appetite was poor, and the patient vomited frequently. At times, when the colicky pains were severe, she could not appeared to be emaciated. Except for the physical appearance and color, the positive findings were confined to the abdomen, which was enlarged, both from bowel distention and from the enlarged uterus extending 2 fingerbreadths above the umbilicus in keeping with the dates. The uterus lay largely to the left of the midline and during the examination contracted strongly at fairly regular intervals. The fetal heart was heard in the lower left quadrant, and a rate of 140 was noted. In the right lower quadrant a fixed, firm, extremely tender mass was observed close to the anterior iliac spine, approximately 6 by 8 cm. in diameter. There was acute tenderness throughout the right side of the abdomen, but there was no referred rebound tenderness. No other organs or other masses could be felt. Peristalsis was intermittent and hyperactive. Rectal examination was not remarkable.

Examination of the blood revealed a red-cell count of 3,250,000, with a hemoglobin of 76 per cent, and a white-cell count of 10,800, with 76 per cent neutrophils. The icteric index was 13. The van den Bergh reaction was 0.3 mg. direct, and the serum protein was 6.6 gm. per 100 cc. The Rh factor was positive, and the blood Kahn reaction

Table 1. *Supportive Therapy in a Case of Terminal Ileitis with Obstruction and Abscess.*

Date	Hospital Course	Supportive Therapy		
		whole blood*	5 per cent glucose†	amigen and 5 per cent glucose‡
		cc.	cc.	cc.
4-12	Patient admitted to hospital.....	—	—	—
4-14		250		
4-15		500	1000 (in normal saline)	
4-16	Patient transferred to surgical service ..	—	—	—
4-17	Miller-Abbott tube inserted	500	—	650
4-18	Operation performed	1000	2000 (in normal saline)	1000
4-19		500	1000 (in distilled water)	1000
4-20		—	1000 (in normal saline) and 1000 (in distilled water)	— 1000
4-21	Miller-Abbott tube withdrawn	500		1000
4-27	Patient delivered		1000 (in distilled water)	1000
5-2	Onset of pelvic abscess	500		1000
5-3		500	1000 (in distilled water)	1000
5-4		—	—	2000
5-7	Abscess drained	—	—	—
6-7	Patient discharged	—	—	—

*One thousand cubic centimeters of whole blood is the equivalent of 146 calories, or 35 gm. of protein.

†One thousand cubic centimeters of 5 per cent glucose in normal saline solution or water is the equivalent of 200 calories, or 50 gm. of glucose.

‡One thousand cubic centimeters of Amigen with 5 per cent glucose is the equivalent of 400 calories, or 50 gm. of glucose and 50 gm. of protein.

retain anything. She was admitted to another hospital 5 weeks later and was discharged after several days' observation, since it was stated that she was improved and presented no evidence of disease. The pain, vomiting and obstipation continued, however, until she re-entered this hospital.

Further questioning revealed that for several months in 1939 the patient considered herself to have colitis. The chief symptoms at that time were frequent loose stools with mucus; there was no blood, abdominal pain or vomiting. The patient continued with her schoolwork. Following this illness, except for a gradual loss of weight, the history was not remarkable until the onset of pregnancy, when difficulty in moving the bowels and ineffectual stools, with some tenesmus, were noted. These symptoms had increased in severity throughout pregnancy. There were also periods of diarrhea accompanied by marked weakness. The patient could remember no tarry or bloody stools. Prior to pregnancy, the appetite, digestion and bowel function had apparently been normal except at the time of the "colitis."

The past history revealed that the patient had never lived in the tropics. There had never been an injury or abdominal operation. The last period had occurred from September 26 to 29, 1944, making the expected date of confinement July 5. The patient had been married for 3 years. The weight in 1936 was 125 pounds, in 1942 115 pounds, in 1944, 102 pounds and at the time of final admission, 98 pounds. The family history was not contributory.

Physical examination on admission revealed a woman who appeared to be severely ill with a chronic disease. The temperature was 98.6°F., the pulse 102, and the respirations 18. The blood pressure was 112/70. There was a slight icteric tinge to the scleras, and the skin was pale and dry. The patient had obviously lost considerable weight and negative. Examination of the urine was negative. The stools were negative for blood and ova.

Three days after admission a barium enema revealed an extensive lesion of the terminal ileum, with narrowing, fixation and distortion of 31 to 41 cm. of bowel. The patient was given 2 whole-blood transfusions, the first being followed by a mild chill and a rise in temperature, — as well as other intensive supportive therapy (Table 1).

On April 17, the patient was transferred to the surgical service, where it was believed that there was an obstructive inflammatory lesion of the terminal ileum. X-ray films revealed passage of barium into what appeared to be a fistula through the bowel wall. The onset of severe pain 2 months before admission was regarded as representing a perforation, and an abscess was believed to be undoubtedly present between bowel loops. Terminal ileitis, tuberculosis, appendiceal abscess and cancer with perforation were considered, the first being the most probable diagnosis. It was believed that surgery was necessary because of the obstruction and the fact that the patient's poor condition precluded expectant treatment. Accordingly a Miller-Abbott tube was passed to relieve obstruction, to decrease the size of the small bowel and give more room at operation, and to relieve pressure on the suture line after operation. The patient was given 0.1 gm. of Nembutal 1½ hours before operation, and 8 mg. of morphine sulfate and 0.3 mg. of scopolamine ½ hour later. Continuous spinal anesthesia was administered as follows: 100 mg. of Metycaine at the start of and 25 mg. during the operation. Whole blood was administered through a cannula in the ankle vein during operation.

At operation on April 18 an ileotransverse colostomy, with exclusion of the involved terminal ileum by transection of the ileum and closure of the distal end, was performed. A

right vertical abdominal incision was made lateral to the rectus, and the structures were divided in the direction of the wound. Exploration of the peritoneal cavity revealed a large inflammatory adherent mass involving the terminal ileum. In addition several loops of ileum proximal to the mass were densely adherent to each other and to the abdominal wall close to the iliac spine. There was considerable injection of the adjacent peritoneum, and exudate was present between the loops of intestine. Approximately 75 cm. of terminal ileum was involved in a typical cicatrizing ileitis with undoubted fistula formation and abscess. The cecum, although somewhat adherent to the mass, was not involved. The ileum was divided between clamps well above the area of the lesion, and the distal end was turned in. The proximal end was anastomosed to the transverse colon, in an end-to-side manner, Young's clamps permitting a closed anastomosis. In the region of the bowel suture and in the wound 6 gm. of sulfanilamide crystals were sprinkled. The abdomen was then closed without drainage.

There was considerable cyanosis postoperatively, the result undoubtedly of sulfanilamide in the abdomen. This rapidly cleared in 24 hours. There was marked improvement in the discomfort and pain in the abdomen. There was little nausea; the bowels moved by themselves on the 2nd postoperative day and freely thereafter. The Miller–Abbott tube was removed on the 3rd day. On the 5th day, however, the icterus index had risen to 55. The serum protein had fallen to 4.3 gm. per 100 cc. in spite of whole-blood transfusions, amino acids and forced protein intake. The urine contained a large amount of albumin and a great deal of bile. It was believed that the jaundice was the result of toxic hepatitis or of other factors, including chronic intestinal disease, acute infection, sulfanilamide and a toxic condition of pregnancy.

The intensive supportive care was continued with adequate fluid, protein and vitamin intake, crude liver extract and progesterone. The daily caloric intake was 2878, which was maintained by food (183 gm. of carbohydrate, 131 gm. of protein and 74 gm. of fat) and by Casec (72 gm. of carbohydrate, 158 gm. of protein and 3.6 gm. of fat). This was supplemented by intravenous injections, as shown in Table 1.

On the 10th postoperative day the patient went into active labor and delivered a living male infant weighing 3 pounds. The baby, however, survived only a few hours.

On the 14th day the patient complained of a sudden severe pain in the lower abdomen that began in the rectum and spread throughout the abdomen. Examination revealed evidence of spreading peritoneal irritation. The patient was apprehensive and in severe distress. The temperature rose to 101°F., and the pulse to 120, and the blood pressure fell to 100/60. It was apparent that some catastrophe had occurred. Perforation of an abscess and leakage at the suture line were considered. In view of the facts that since operation there had been no evidence of reaction about the anastomotic and transection sites and that the onset of this disturbance was in the pelvis, it was decided that pelvic peritonitis from the inflammatory mass was the likeliest diagnosis. Supportive treatment with blood and penicillin were begun. After several hours the patient improved and localization in the pelvis began to take place. Five days later a pelvic abscess was evacuated through the vagina. From this point on improvement was rapid. The abdominal incision healed by first intention. The patient gained strength rapidly and was discharged from the hospital on June 7.

At the time of a check-up examination on September 20 the patient weighed 110 pounds, felt extremely well, and had an excellent appetite. There was no indigestion or abdominal pain. The bowels moved 3 times daily; the first movement was formed and was followed in a few minutes by 2 small loose dejections. The gas pains, abdominal distress and bowel disturbance, which had been present during pregnancy, had completely disappeared. The periods were normal. Examination disclosed a marked improvement in appearance. Abdominal examination revealed a well healed scar. There was no tenderness or masses. Only slight thickening could be felt in the right iliac fossa. Pelvic examination was negative, as were blood and urine studies. X-ray films disclosed that irregularity and narrowing were still present in the excluded loop of terminal ileum, but repeated plates and fluoroscopy during passage of a barium meal showed no other bowel lesion. The anastomosis functioned well, and there was no tenderness, dilatation or further irregularity.

A final report from the patient on August 1, 1946, indicated that she remained well and weighed 117 pounds.

Discussion

Surgery in ileitis is undertaken for patients with obstruction, fistula or abscess or who are unable to maintain weight and strength with reasonable freedom from symptoms under adequate medical management. Acute nonobstructive lesions in the early stages should not be disturbed, since the etiology is unknown and recurrence is frequent. The exclusion operation, as performed in the case presented above, yielded excellent results in the hands of Garlock and Crohn, who reported 164 cases followed for from two to fourteen years with the low operative mortality of 8.5 per cent.[7] Resection in one or two stages has been advocated and practiced by many authorities, including Cave[7] and Bockus.[8] Marshall,[9] at the Lahey Clinic, utilized obstructive resection with excellent results.

In the case reported, there was no choice regarding the type of surgical procedure. The involved loop was so completely fixed with inflammatory reaction that resection was completely ruled out. Following the exclusion operation improvement was so marked that further surgery was hardly advisable.

The management of abdominal surgical complications in pregnancy is always an extremely interesting and frequently a difficult problem. Phaneuf[10] and De Lee[11] state that in cases in which operation is necessary the pregnancy should be disregarded. If delay is safe, postponement of operation is advisable. In cancer the questions of obstruction, operability and viability must be considered in each case. Occasionally, in intestinal obstruction, hysterectomy is essential, to disclose obstructive points hidden by the uterus.[4] Cesarean section may be necessary in the true ileus of pregnancy.[4]

In the above case operation to relieve obstruction and to maintain life was urgently needed. It is evident from the pathologic state in the abdomen and the cachectic condition of the patient that an attempt to carry this patient on an expectant regime until viability was assured, with subsequent induction of labor, would have been fraught with grave danger to the mother. Certainly, maintenance of balance of nutrition would have been difficult or impossible for more than a few days without relief of obstruction, even with the aid of intestinal intubation. Accordingly, the pregnancy was ignored, and the short circuiting and exclusion procedure accomplished. Premature labor was almost a certainty, for vigorous contractions, indicating uterine irritability, were present from the time of hospital entry. Slemons and Williams[5] and Phaneuf[10] state that labor follows in a high percentage of such cases. In intestinal obstruction there is usually a

maternal mortality of 40 per cent and a fetal mortality of 65 per cent.

This case illustrates the importance of abdominal pain in pregnancy, as well as the necessity of intensive and continued preoperative and postoperative care because of possible surgical complications and nutritional requirements. Incidental points of interest were the occurrence of jaundice and the rapid drop in serum protein values in the immediate postoperative course in spite of administration of large quantities of protein. The acute hepatitis undoubtedly interfered seriously with protein metabolism.

Continuous spinal anesthesia was probably of considerable value. It permitted a controlled anesthesia, produced by small quantities of drug at intervals, so that reactions could be avoided, excellent relaxation maintained, and time afforded for an accurate, gentle and meticulous procedure.

Summary

A case of obstruction and abscess secondary to terminal ileitis in the seventh month of pregnancy is reported.

The unusual occurrence of severe obstructive ileitis in pregnancy is noted.

Certain aspects of the surgical management of the patient are briefly discussed.

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MEDICAL PROGRESS

PRESENT CONCEPTS OF BENIGN BREAST DISEASE (Concluded)*

IRA T. NATHANSON, M.D.†
BOSTON

CYSTS, HYPERPLASIAS AND PAPILLOMAS

The greatest difficulty in interpretation and classification is encountered in lesions that exhibit cysts, hyperplasias or papillomatous formation. The lesions frequently coexist with or are superimposed on the abnormalities described above. Thus it can be seen that the opportunity to designate some lesions as distinct entities is relatively rare. It is probable that the various changes are manifestations of the same syndrome, but the evidence is not conclusive. The lesions usually occur in women in the latter part of active sexual life. Unlike the syndromes described above, regression following the menopause appears to be less frequent, but this cannot be stated with certainty since observations are based entirely on patients who consult a physician. Cyclic swelling and objective symptoms other than the presence of isolated or diffuse lumpiness of the breast are conspicuously absent. The syndromes seem to occur more frequently in childless women, and coexistent pelvic disease is not unusual.[3] The physical findings vary considerably and are difficult to define in many cases. For the purpose of clarification the lesions are described on the basis of the dominant histologic findings, even though other changes are found elsewhere in the breast.

Macroscopic Cysts

The solitary cyst or multiple cyst of similar origin and the so-called "blue dome" cyst of Bloodgood and others are easily distinguished. As Foote and Stewart[13] pointed out, the lesions designated under this heading should be included only if they are isolated structures — that is, visible to the naked eye (1 mm. or more in size) — and distended with fluid and totally separate from the duct and lobule systems. It is further stressed that a diagnosis of microscopic cysts requires serial sections to prove complete isolation and loss of communication with the adjacent ducts or lobules. Lesions often appear cystic but are actually dilatation of the duct system or acini. Macroscopic cysts vary considerably in size, and if large enough, are tense to palpation. Epithelial linings are frequently absent, and hyperplasia is rarely found, even when the linings can be distinguished. Intracystic papillomas and carcinomas are unusual.[13] As a rule, lesions that appear to arise in cysts must be considered intraductal unless proved otherwise by serial section.

Hyperplasias

Epithelial hyperplasia in the duct systems and acini may occur with or without cysts. The degree of the proliferative process varies considerably in the same breast and may be palpated as a localized nodularity or as a diffuse process, usually of "doughy" consistence and with associated areas of irregular nodularity. Dilatation associated with blockage of the duct or lobule component by the proliferative lesion may resemble true cysts. Secretion, either serous or serosanguinous may occur. These lesions resemble those originally described by Reclus.[31]

Papillomas

There is no sharp distinction between the simple hyperplasias and the more marked types resembling and tending to papillomatous formation. Frequently all stages of hyperplasia are seen in the same breast, and at times an apparent transition to papillomatous formation can be distinguished. For this reason many observers are of the opinion that these lesions are advanced stages of the simpler processes. Thus, a division based on the degree of hyperplasia must be arbitrary. Included under the designation of papillomas are the obvious and gross papillary lesions, with a definite stalk found in the larger duct systems, and microscopic lesions involving the smaller duct systems manifested by marked epithelial hyperplasia with papillomatous features and without obvious evidence of a stalk. Various degrees of papillomatous change are seen in the same breast, and may be associated with macroscopic cysts or duct or acinar dilatation or both.

The gross papilloma, which may be multiple, usually appears near the duct opening in the region of the areola and, although infrequently palpated, can sometimes be detected by transillumination and gross thickening of the proximal duct system involved and by mammography. Discharge from the involved duct is often seen and is usually serosanguinous in contrast to the fluid noted in other lesions. Occasionally the ducts containing gross papillomas can be identified by systematic palpation around the areola and by application of pressure at various points to elicit a discharge.

Microscopic papillomas are almost invariably found elsewhere in the breast in the presence of a

*From the Medical Laboratories of the Collis P. Huntington Memorial Hospital and the Tumor Clinic of the Massachusetts General Hospital, Boston, and the Pondville Hospital (Massachusetts Department of Public Health), Walpole, Massachusetts.
This is publication No. 620 of the Harvard Cancer Commission and No. 116 of the Pondville Hospital.
†Associate in surgery, Harvard Medical School; assistant surgeon, Massachusetts General Hospital and Pondville Hospital.

gross papilloma. Physical findings, although sometimes more pronounced, are essentially the same as those observed in breasts with only epithelial hyperplasia. The syndrome is consistent with that described by Schimmelbusch.[32]

Other Lesions

Foote and Stewart[13] have described and introduced new terms for several other lesions that appear to be distinctive. Although, as they point out, such terms may be undesirable, it is believed that this terminology should be encouraged, inasmuch as it stimulates interest and demands more specific interpretations of lesions that are frequently seen but poorly understood. These terms include the following.

Blunt duct adenosis. In this manifestation, the duct ends abruptly near its distal portion without termination in lobules. The lumens are usually narrow, and the epithelial lining varies from simple hyperplasia to that resembling papillomas in the earlier stages. The advanced stages are characterized by dilatation and flattening of the epithelium. All degrees of change may be seen in a single breast. The process may exist as a single focus or as a palpable mass of nodularity, especially when lobules are absent and small cysts possibly arising as an end result of blunt duct adenosis are numerous.

Aprocrine epithelium. Large, tall, cylindrical cells possessing relatively small nuclei and abundant, bright eosinophilic cytoplasm are characteristic of aprocrine epithelium, aggregates of which grossly present a discrete yellowish-brown appearance of slightly elevated, glistening areas, small in diameter; larger aggregates may be cystic as well.

Sclerosing adenosis. This abnormality may be manifested as an early florid phase, characterized by epithelial proliferation, an intermediate phase and a late phase in which fibrous elements are dominant. It may appear as a grossly localized mass or more frequently as focal areas seen only on histologic examination. The lesions usually arise in terminal ducts or lobules.

Lobular alteration. Primary and secondary types have been distinguished. For a complete discussion one is referred to the original study.[13] In primary lobular alteration, as a rule, there is homogeneity of structures. The following three types, which are similar to adenofibrosis, are usually seen: a small number of lobules condensed with small, scanty acini and fibrous stroma often replaced by fat; an average number and size of lobules, with abundant, loose and edematous connective tissue and few but large and piled up epithelial components; and an irregular — that is, heterogeneous — lobule pattern that in some cases exhibits epithelial activity and in others appears to be undergoing regression, with evidence of atrophy and cystic formation. In secondary lobular alteration, lobules adjacent to a mass — such as cysts, fibroadenomas and cancer — exhibit interlobular edema, changes in contour and size, epithelial components and round-cell infiltration; as the primary lesions progress or persist, however, all degrees of change are noted until the lobules are obliterated, edema disappears and round-cell infiltration is predominant.

Objective evidences of these newly designated microscopic lesions are difficult to define. By correlation of clinical and histologic observations, however, it is likely that they will be clarified.

It is necessary to emphasize again that the lesions discussed under the term "chronic cystic mastitis" are not necessarily separate entities, but may coexist in any combination to complete the general picture.

Relation of Benign Lesions to Carcinoma

This problem has been discussed elsewhere,[3, 13, 28–30] but the increasing statistical and histologic observations warrant additional evaluation. It is becoming increasingly apparent that certain lesions are apt to be associated with or to precede cancer of the breast whereas others are equivocal or may be of no significance. The more thorough studies indicate that adenofibrosis,[29] fibroadenomas[13, 29] and macroscopic cysts[13] are less often seen in conjunction with cancer of the breast. Other lesions included under chronic cystic mastitis are more difficult to evaluate. These manifestations, which have a greater tendency to be associated with carcinoma, are marked epithelial hyperplasia,[29] papillomatosis[13, 29] and, possibly, blunt duct adenosis.[13] As pointed out by several observers, the papillomatous lesions, especially when atypical, precede or coexist more frequently with carcinoma.[13, 29] In some cases transition from the benign state to the neoplastic process can be demonstrated.[13] An appraisal of the situation with a broad point of view indicates that any of the abnormalities alluded to — with the possible exception of fibroadenoma — may precede or coexist with malignant change in the breast. Some are obviously of a special significance, but as yet they cannot be defined with certainty. For the moment the question is still open, but it is expected that studies will continue to elucidate this fundamental problem.

Benign Breast Disease in the Male

As in the female, certain benign disease of the male breast is erroneously designated mastitis. The term mastitis should be used only for specific inflammatory processes that are rare and apparently bear no relation to the lesions usually seen in the male. Gynecomastia is also used by some observers as a general term to describe the common forms of benign breast disease in the male, but it should be reserved for a special group as pointed out below. For these reasons, the term "mammoplasia" is

suggested to describe the benign noninflammatory processes, which are transient in character and as such are distinguished from gynecomastia. It is realized that introduction of another term into an already confused field may be undesirable, but it is believed justifiable in view of advances made in the concepts of breast disease in general.

Adolescent or Pubertal Mammoplasia

This condition, which in the male is akin to the changes seen normally at the onset of breast development in the female, usually appears between the twelfth and seventeenth years and is characterized by the presence of a well defined, freely movable, discoid mass beneath and closely associated with the areola. The mass varies in size from less than 1 to 5 cm., but as a rule is 2 or 3 cm. The nipple and areola may also be increased in size. The process is usually unilateral at the onset, but may affect both breasts, simultaneously or successively.[33] It occurs more frequently than is generally recognized. Jung and Shafton[6] in approximately a thousand examinations found that it was an integral part of the process of puberty. It is not seen oftener because of the frequently transient character of the process, which may arise and regress within even a month. Histologic examination reveals lengthening and hypertrophy of the ducts, with an increase in periductal connective tissue. Lobule formation is usually absent. In a small percentage of cases this lesion persists and may then be correctly called gynecomastia. A process similar to adolescent mammoplasia is seen in postadolescent males. A number of cases were reported in soldiers in World War II. Few, if any, had a history of previous breast trouble so that the process may well be similar to that noted in the adolescent.

Gynecomastia

In gynecomastia the contour and elements of the breast approach those of the normal woman. As stated above the abnormality may represent a persistence of the adolescent type or may arise spontaneously in the adult or in the presence of associated diseases. It may be unilateral or bilateral. Histologically, in addition to the changes described above, there may be hyperplasia of the duct epithelium, dilatation of the ducts and occasional secretion. The presence of acini and lobules is rare. The main differences from the other types of benign breast disease in the male are the persistence and the physical characteristics.

Senescent Mammoplasia

After the age of forty-five years, but particularly after sixty, changes resembling those seen at puberty are frequently encountered. Some, of course, occur earlier. The disease behaves in a fashion similar to that seen in the youth, but spontaneous regression is not so frequent.

Etiologic Factors

There are no obvious associated abnormalities in the large majority of these cases. Adolescent and senescent mammoplasia, as noted, occur at the extremes of active sexual life. It is possible, therefore, that at these periods there is a temporary hormonal imbalance. Both mammoplasia and gynecomastia, however, occur in association with other diseases and in such cases possible etiologic factors are apparent. These may be described as follows:

Atrophy of the testicle following orchitis or injury. The spermatic tubules are frequently atrophied, and the atrophy thus accompanied by a relative or actual increase in the interstitial cells. Since these cells are supposedly the site of origin of androgens, it is possible that they are responsible for the change in the breast.

Neoplasms of the testes. Mammoplasia and gynecomastia are sometimes associated with tumors of the testes, particularly chorioepithelioma. Gilbert[34] is of the opinion that the breast lesions are of two types — a "physiologic," resembling the usual mammoplasia in males and not necessarily related directly to the tumor of the testes, and a "choriogenic," most frequently related to the chorioepithelioma and resembling the female breast in its histologic characteristics, especially during pregnancy. The pituitary gland in cases with choriogenic gynecomastia shows changes that are also seen in pregnancy. In contrast to the physiologic type, these lesions may be caused by the hormones secreted by the tumor itself. Several cases of gynecomastia have also been associated with interstitial-cell tumors of the testes.[35] The nature of the stimulus in these cases is not clear, for although one would expect the androgens to be in excess, 1 patient had loss of libido suggesting destruction of testicular function and failure of the tumor to secrete a hormone to maintain such a function.

Functioning tumors of adrenal cortex. These tumors may produce feminization, in contrast to the usual masculinizing syndrome seen in females and prepubertal males.[36,37] The syndrome is characterized by mammary enlargement, regression of secondary sex characters and atrophy of the testes. Since estrogens as well as androgens have been recovered from the adrenal gland and because elevated excretion levels of both these substances are frequently found in patients with adrenocortical tumors, a hormonal cause seems evident, especially since removal of the tumor is followed by regression of the breast lesion.

Hypophyseal adenoma.[38] These lesions may give rise to atypical pituitary secretion affecting the breast directly or indirectly as a result of stimulation of the peripheral endocrine organs.

Cirrhosis of liver. Breast changes associated with cirrhosis are sometimes encountered.[39] The

patients often show testicular atrophy. It is conceivable that the breast lesions may be caused by faulty metabolism of the hormones as a result of the cirrhosis, since the liver is intimately concerned with such a metabolism. An alternative possibility is a loss of testicular function.

Syndrome of unknown cause. A syndrome characterized by aspermatogenesis, testicular atrophy and gynecomastia without known cause has been reported by Klinefelter and co-workers.[40] The testicular changes resembled those seen after orchitis or injury, and may possibly fall into the same category.

Other conditions. The mechanism involved in the production of mammoplasia in patients with thyrotoxicosis,[41] leukemia and pulmonary carcinoma, as well as in soldiers with malnutrition or debilitating diseases,[42] is not clear. It seems, however, that in these diseases there is also a disturbance of the metabolism of the hormones.

Hormonal induction. Mammoplasia of a transient character develops in eunuchs following the injection of testosterone.[43, 44] Such treatment is followed by an increased excretion of estrogens in the urine and suggests, therefore, a metabolism or conversion of the androgens to estrogenic substances.[45–47] This may be characteristic for the eunuch, since such changes after administration of androgens to a normal person are exceedingly rare. As would be expected the administration of estrogens to the male for various causes — especially carcinomas of the prostate gland — results in mammary hypertrophy.[48–51] The nipples and areola enlarge, and in some cases there is marked epithelial proliferation and acinar formation. Interestingly enough, I have observed unilateral or asymmetrical response after estrogen therapy. Such a finding is consistent with the concept of differential tissue sensitivity. Removal of the stimulus results in relatively rapid regression of the process. Excretion studies of gonadotropic and sex hormones in the urine have been fully described elsewhere.[3]

Benign breast disease in the male seems to be associated with an endocrine imbalance, either as a result of sexual metamorphosis or of an associated abnormality or tumor. Since the changes normally produced by the various hormones are not identical, clarification may come when a careful correlation is made between the histologic appearance of the breast and a known activating agent. A common denominator may be found in the so-called "mammogenic hormones,"[3] which may be activated by either estrogens or androgens. Hence, similar lesions could be produced by these different hormones. Most of the available data point to the estrogens as an important factor. Changes induced in the breast by the administration of estrogens are frequently seen, but except in the eunuch testosterone seldom produces obvious breast abnormalities. Moreover, testosterone has been used with success in the treatment of the more transient types of mammoplasia. These paradoxical findings may possibly be explained by a difference in the metabolism of the hormones as a result of disease or variation in the endocrine status.

Discussion

The available clinical and experimental information emphasizes the significance of the endocrine system in the development and growth of the mammary gland. The ovary and hypophysis are especially important, for without one or the other breast development does not occur or ceases entirely. Furthermore, removal of these organs leads to regressive changes in the fully developed breast. Thus, it has been contended that disease of the breast is definitely related to or caused by alterations of function or secretion of certain glands of internal secretion. Factual data, for such a thesis, have been reviewed elsewhere.[3] A general discussion of the possibilities involved seems necessary, however, since certain factors are common to all types of breast disease.

Factors other than endocrine must be considered in the development of breast disease. Chief among these are heredity, race, color and constitutional type, which are frequently interrelated but may be individually of special significance. Although the evidence to support these possibilities is far from conclusive, one may justifiably speculate on them. Physiologic status, endocrine metabolism and secretion and susceptibility to the disease may depend to a considerable degree on these fundamental backgrounds. These basic states in some measure may thus determine the type and degree of response of the organism to normal or superimposed stimuli. This would help to explain the variety of changes in the breast that have been attributed to the same agent, such as estrogens.

The stage of life and state of the breast when abnormalities appear may also determine the type and degree of response to a given stimulus. It has been shown that the histologic structure and clinical manifestations of diseases that arise during various age periods vary considerably. Moreover, the degree of development and structure of the breast may differ regardless of age as a result of variations in physiologic status. Dieckmann[8] has shown that the extent of development of the breast, particularly at puberty, is subject to wide variation among different persons. Previous pregnancies and normal and abnormal lactation account for breast changes not encountered in the virgin female. Other processes, such as inflammatory disease, may likewise alter the state of the breast. Thus, the breast may exhibit wide varieties of histologic structure under different conditions, and these dissimilar substrates may therefore vary considerably in their response to a

single stimulus and may determine to some degree the abnormal changes that subsequently appear.

Foremost among the probable stimuli responsible for breast disease are those of the endocrine and nervous systems. The hormones that have been the subject of the most intensive study are the estrogens. Nevertheless, the possibilities suggested by investigations may apply to other hormones as well. How may estrogens produce these atypical states? Several possible modes of action seem tenable. Physiologic amounts of the hormone may act on tissue that is more sensitive than normal. This susceptibility may be related to the metabolic status of the host, to special characteristics of the cells, or to a change in the breast as a result of the activity of other agents. It has been demonstrated that estrogens are destroyed by the liver. Normal quantities of the hormone may be secreted, but because of defective function of the liver, abnormal quantities may be released to the tissues. Excessive quantities of the hormone may be responsible, but, except in cancer-susceptible animals, the effects are limited. Atypical hormones with carcinogenic activity may be produced. This is possible since the steroid hormones are closely allied to several of the known synthetic carcinogens. It is conceivable that the formation of carcinogenic agents from hormones may occur as a result of a faulty metabolism due to a change in the physiologic state of the host. Lack of a hormone, which normally stimulates the breast, may lead to degenerative or regressive changes that may then allow other agents to act.

As has been pointed out, the nervous system may also be involved. The action may be direct, but it is more probable that such stimuli exert their effect by causing excesses or alterations of hormonal secretion. Furthermore, the close interrelation of the various endocrine organs suggests that disturbance of one organ could affect the function of the others. Because of the possible methods of action or alterations of hormonal secretion, there is still lack of conclusive evidence to justify the acceptance of any one factor.

As suggested above, the state of the breast at the time that an abnormal stimulation is superimposed is probably of some importance. Infantile and virginal hypertrophy, early ripening, adenofibrosis, fibroadenomas in the female and gynecomastia and mammoplasia in the male are remarkably similar in histologic appearance and in their resemblance to changes usually seen in the normal adolescent female. It is conceivable, therefore, that they may be due to the same etiologic agent, possibly the hormones. Lewis and Geschickter[61] emphasized this similarity in virginal hypertrophy, gynecomastia and fibroadenoma, and there is fairly good evidence to support such an opinion. The different forms of disease classified under the present accepted designation of "chronic cystic mastitis" also basically resemble each other, in spite of considerable variation in the individual case.

It has repeatedly been stressed that lesions described above as possible entities may coexist in the same breast. This suggests that each type may represent a later stage of or may be superimposed on the same basic abnormality. The changes may represent manifestations of quiescence or stimulation as indicated by involutions or proliferations that in part may have occurred prior to the time of examination. Thus, this point of view reverts to the thesis that localized areas of the specific tissue are unusually sensitive to a stimulus. It is my opinion that this sensitivity is a major determining factor in the production of the heterogeneous groups of lesions described.

In almost all types of breast disease — from the simple infantile hypertrophy to complex breast cancer — there is a suggestion of some dysfunction of the endocrine system in many cases. Nevertheless, it can be stated that evidence is insufficient to support the thesis that the hormones themselves are directly responsible for the production of benign and malignant lesions. It is possible, however, that they may be exciting factors or may prepare a suitable substrate and thus contribute to the initiation and production of the varieties of breast disease.

As a result of increasing knowledge and clarification of lesions of the breast, concepts have changed in the last decade regarding management of benign disease. A solitary mass or a localized nodularity, as has been repeatedly emphasized in all teachings on breast disease, must be investigated surgically, since it is often impossible to distinguish between clinically benign lesions and early cancer. Obviously, radical mastectomy must be performed if the lesion proves to be cancer. The removal of a localized benign process may be all that is necessary, particularly in young women. Thereafter, systematic observation should be instituted.

Benign lesions except for the so-called "precancerous hyperplasias" are of significance so far as they cause annoying symptoms or exert an unfavorable psychologic effect on the patient. It is the responsibility of the physician to decide on the proper management in the individual case. This demands, therefore, an objective view based on a broad comprehension of breast disease. Since many of the lesions are diffuse one is faced with the choice of conservative management or a simple mastectomy, if the indications warrant it, as a preventive measure against cancer. The majority of benign diffuse processes frequently involve both breasts, and it therefore seems illogical to perform unilateral simple mastectomy as a prophylaxis against cancer. Warren[29] states that if an excised focus of chronic cystic mastitis shows evidence of definite precancerous hyperplasia, a simple mastectomy should be performed. He believes, however, that there is not sufficient risk of subsequent develop-

ment of carcinoma in the remaining breast to warrant or justify bilateral mastectomy as a rule. It is my conviction that simple mastectomy is performed too frequently for benign lesions of the breast.

Conservative management and reassurance is all that is necessary in handling the syndromes of adenofibrosis and nonpuerperal secretion, in the absence of a localized mass. So far as cystic disease is concerned, the process is often diffuse. It is not unusual to find additional cysts arising after a solitary lesion has been removed surgically. The surgeon is therefore faced with the problem of another or repeated excisions, simple mastectomy or conservative management.

Solitary large cysts may be aspirated with considerable safety, since the possibility of cancer within the lesions described is relatively remote. As a rule, however, these lesions recur, and surgical intervention is necessary for eradication. If multiple cysts are found and the diagnosis is verified by aspiration or local excision of a typical lesion, careful observation in a majority of cases will accomplish the same effect in the end as a radical procedure. In young women particularly the psychologic effect of simple mastectomy may be profound; in older women there is less emotional reaction to the procedure.

When one is faced with the more complex structures — particularly those of precancerous hyperplasia or papillomatous change — the problem becomes increasingly difficult. In the single gross papilloma, excision of the entire duct system may be all that is necessary. The gross lesions may be multiple, however, so that every effort should be made to identify them. If the papillomatous process is diffuse or atypical or if precancerous hyperplasias exist, it is probably wiser to carry out simple mastectomy as a prophylactic measure because of apparently close association with cancer.

Conclusions

The endocrine organs and their secretions are necessary for normal growth, development and maintenance of the mammary gland. As such, they are indirectly responsible for breast disease, since they provide the tissue in which the lesions arise.

Factors such as heredity, constitution, race, color and physiologic state of the patient must also be considered causes of breast disease.

The state of the breast at the time of onset of disease seems to be an important factor in the type of lesion seen. A single stimulus may thus produce a variety of apparently different lesions.

Localized tissue susceptibility may account for an unusual response to an apparent normal stimulus.

Endocrine dysfunction is frequently associated with and may be responsible for certain benign lesions, but there is no absolute proof that it is the only or direct etiologic factor.

A number of histologic lesions classified under the general term of chronic cystic mastitis may be distinct entities, but they frequently coexist in the same breast.

A revised classification of breast lesions and a recognition of these as distinct entities is essential to a better understanding of etiologic factors and to intelligent management of the individual case.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 32411

PRESENTATION OF CASE

A sixty-nine-year-old unemployed woman, formerly a practical nurse, entered the hospital because of palpitation.

The patient had been in good health until two and a half years before admission, when she first noted shortness of breath and palpitation after mild exertion. From then on exertional dyspnea progressed steadily until she was unable to do more than walk about her room without precipitating an attack. During the same interval, orthopnea developed and there were occasional attacks of nocturnal dyspnea, usually of no more than fifteen minutes' duration. Palpitation was always a prominent symptom, occurring at first only following exertion but later during bed rest. For six months there had been a constant, increasing coarse tremor of both hands and arms. Slight numbness and tingling of the fingers had appeared during the previous two months. Nocturia (two or three times) and frequency during the day appeared in the course of the illness. There was never any swelling of the hands, face, abdomen or ankles, or any precordial pain, oppression or convulsive seizures. Three days before admission the patient fainted, falling across the bed. Several minutes after she regained consciousness there was a spontaneous brisk nosebleed, which lasted several minutes. She noticed no visual changes or muscular weakness on recovery. She had never had hypertension. During the two and a half years of illness there had been progressive anorexia, accompanied by a 55-pound weight loss. Muscular weakness was a prominent symptom.

For three months after the onset of the symptoms the patient had been given digitalis by a physician but had subsequently received none. For two years she had received weekly injections of liver and many iron tablets. Three months before admission 20 drops of iodine solution was administered three times daily, and the patient thought that she felt stronger for a time.

As a child the patient had had aches first in one knee and then in the other that lasted several days. The joints were not swollen, and she was not put to bed.

Physical examination revealed a thin, pale woman exhibiting a marked coarse tremor of the hands and lips. The face bore a masklike expression. The skin was dry and warm. The arms and legs were wasted and weak. There was slight exophthalmos, lid lag and infrequent blinking. The thyroid gland was slightly enlarged and nodular. A Grade III systolic and a harsh mid-diastolic murmur were heard at the apex, and there was a Grade II or III systolic murmur in the aortic area. Flatness, decreased breath sounds and decreased tactile fremitus were elicited at the left lung base. The liver edge was palpable three fingerbreadths below the costal margin. The tremor of the hands was more marked on intention. Pelvic examination revealed tenderness in both vaults; no masses were palpable. There was tenderness over the lumbar spine and sacrum.

The temperature was 98.0°F., the pulse 95, and the respirations 20. The blood pressure was 110 systolic, 58 diastolic.

Examination of the blood showed a red-cell count of 1,890,000, with a hemoglobin of 6.7 gm., and a white-cell count of 11,800, with 94 per cent neutrophils. The hematocrit was 19 per cent. The nonprotein nitrogen was 140 mg., the total protein 7.2 gm., with a normal albumin-globulin ratio, the blood sugar 108 mg., and the calcium 9.6 mg. per 100 cc. The basal metabolic rate was + 11 per cent. The specific gravity of the urine was 1.006, and there was a + albumin reaction; the sediment contained 3 white cells and 1 epithelial cell per high-power field. A stool was brown and gave a ++++ guaiac test.

On x-ray examination the heart appeared enlarged on both sides and also in the anteroposterior diameter. The aorta was extensively calcified from the arch to the iliac arteries. The left pleural cavity contained a moderate amount of fluid, and there was a small amount on the right. An electrocardiogram showed inverted T_1, T_{CF4}, and T_{CF5}, prominent S_3, upright T_2, T_3 and T_{CF3} and depressed ST_{CF4} and ST_{CF5}. The rhythm was normal.

The patient was slightly short of breath, slightly orthopneic and extremely weak but had no specific complaints. Barium studies of the upper gastrointestinal tract showed the esophagus displaced to the right and posteriorly, apparently by the left auricle (Fig. 1). The stomach and duodenum were normal except for a pressure defect produced in the latter by the gall bladder. The severe anemia did not improve. White cells up to 20 per high-power field appeared in the urine, which was otherwise unchanged.

On the fourth hospital day the patient suddenly sat up in bed and expired.

DIFFERENTIAL DIAGNOSIS

DR. RULON W. RAWSON: May we see the x-ray films?

DR. JAMES R. LINGLEY: The heart shows marked generalized enlargement, without characteristic configuration. The lung fields are clear, but there is fluid at both bases, more marked on the left than on the right. The esophagus is displaced, as described in the record, apparently by this enlarged left auricle. I think that that goes along with the general cardiac enlargement. On this lateral view there is also a ring of calcification in the heart, which corresponds to the annulus of the mitral valve. There is an extreme degree of calcification in the aorta; apparently it extends the entire length from the heart to the bifurcation.

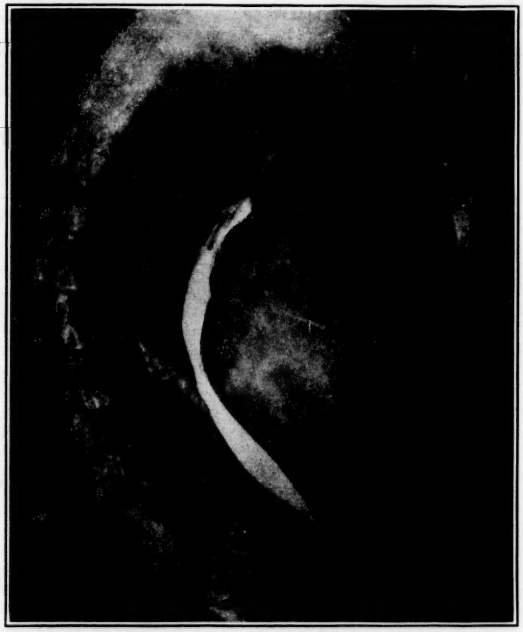

FIGURE 1. *Lateral Chest Film, Showing Generalized Aortic Calcification, Calcification of Mitral Annulus and Pressure Displacement of Esophagus by Left Auricle.*

DR. RAWSON: It is impossible for me to ascribe this entire picture to one disease entity. The diagnosis of old rheumatic heart disease seems a sure bet. The history of the joint pains in childhood suggests it, and the Grade III systolic and the mid-diastolic murmurs at the apex are also suggestive of that. The x-ray finding of enlargement of the heart on both sides in the anteroposterior diameter, with displacement of the esophagus to the right by what was thought to be an enlarged left auricle, makes the diagnosis almost certain. The aortic systolic murmur can be explained by rheumatic heart disease, but can likewise be explained by arteriosclerosis and the calcified aorta that Dr. Lingley has shown us.

Dr. Bland tells me that the electrocardiographic changes are consistent with coronary heart disease and some old infarction but states also that it could be explained on the basis of anemia. The finding of fluid in the chest can be adequately accounted for on the basis of cardiac failure, as can the enlargement of the liver, although enlargement of the liver could also be explained by some other diagnostic possibilities, which I shall discuss.

In view of the weight loss, the tremor, the palpitation, the lid lag, the exophthalmos, the warm skin and the symptomatic improvement following the administration of iodine one has to think of Graves's disease. The weight loss can be explained on the basis of anorexia. The tremor was a coarse one. As a rule the tremor in Graves's disease is fine and rapid. Frequently in older people we do see a

coarse tremor, which is rapid, however. There is no statement whether or not this tremor was rapid. I should prefer to attribute it to weakness. The palpitation could also be explained on the basis of thyrotoxicosis, but I think that it is adequately accounted for on the basis of heart disease and the anemia. Enlarged liver does occur with long untreated Graves's disease, but again is adequately explained on the basis of heart failure. The eye signs, the goiter and the subjective improvement on the administration of iodine are strongly suggestive of Graves's disease. The basal metabolic rate, however, was only +11 per cent, which is quite low for a patient this ill with thyrotoxicosis, especially in the presence of heart failure. Usually patients with heart failure have elevated basal metabolic rates, whether or not they have thyroid disease. It is of interest that a number of years ago in an analysis of patients in this hospital who had heart disease and on whom total thyroidectomies were done, it was found that frequently when they returned to the hospital or clinic in a state of decompensation the basal metabolic rate was elevated as high as +20 to +25 per cent, and that when compensation was restored and the fluid removed, the basal metabolic rate fell to —20 per cent or lower. So I am skeptical of the diagnosis of Graves's disease with a basal metabolic rate of only +11 per cent, especially with cardiac decompensation. We have seen a few patients, however, who entered the hospital with thyroid storm and who were so debilitated that had we been able to determine the basal metabolic rates, it is possible that they would have been found low. It should be pointed out that neither the cardiac failure, the decompensation nor the hyperthyroidism can account for this degree of anemia. Also, it is important to recognize that the white-cell count of 11,800, with 94 per cent neutrophils, is not a classic picture for Graves's disease. Usually there are leukopenia and lymphocytosis.

The anemia was hyperchromic. The color index was 1.25, with a mean corpuscular volume of 1, and therefore one should consider the diagnosis of pernicious anemia. The anorexia for two and a half years and the ++++ guaiac reaction in the stool make one look at the gastrointestinal tract as a source of blood loss, and as a cause of this particular type of blood picture. A malignant growth in the cecum or stomach could produce this type of blood picture. Since the radiologist found no evidence of disease in the examination of the stomach one is likelier to look at the cecum for the primary lesion. I think that the last case I discussed before this group, however, was a case of carcinoma of the stomach with a positive guaiac reaction in which the radiologist considered the examination of the stomach to be negative. The negative x-ray examination certainly does not rule out cancer of the stomach. The pressure defect in the duodenum was said to have been due to the gall bladder. One might also suggest that this was a peritoneal lymph node, and therefore one should consider the possibility of lymphoma, probably of the abdominal type. The patient had no fever, however, which speaks against Hodgkin's sarcoma or abdominal lymphoma. A lymphosarcoma of the stomach or bowel is a possibility.

I think that the fainting episode three days before admission can be accounted for on the basis of a large gastrointestinal hemorrhage. Since the total blood protein of 7.2 gm. per 100 cc. following what I think was a hemorrhage seems rather high, one should list plasma-cell myeloma as a possibility. The nonprotein nitrogen of 140 mg. per 100 cc. merits comment. I think that it can be explained on the basis of cardiac failure, gastrointestinal bleeding and arteriosclerosis. The sudden death could have been due to embolism or a massive gastric hemorrhage.

My first diagnosis, therefore, is rheumatic heart disease, with mitral stenosis, aortic stenosis, arteriosclerosis and cardiac decompensation. I shall list as my second diagnosis cancer in the gastrointestinal tract, probably carcinoma of the cecum.

DR. TRACY B. MALLORY: The level of the nonprotein nitrogen apparently does not bother you, Dr. Rawson.

DR. RAWSON: The patient may have had an old nephritis. The arteriosclerosis probably involved the kidney, however. Also, she quite likely was in shock, which would explain in part the elevated blood nonprotein nitrogen.

DR. WALTER BAUER: Certain findings suggest the possibility of multiple myeloma, but there is nothing that you can "hang your hat on" with certainty.

CLINICAL DIAGNOSES

Uremia.
Anemia.
Generalized arteriosclerosis.
Coronary heart disease.
Old rheumatic heart disease, with mitral stenosis.
Chronic nephritis.
Carcinoma of bowel?

DR. RAWSON'S DIAGNOSES

Rheumatic heart disease, with arteriosclerosis, mitral and aortic stenosis and cardiac decompensation.
Carcinoma of cecum.

ANATOMICAL DIAGNOSES

Acute rheumatic myocarditis.
Calcification of aortic and mitral valves and of annuli of aortic, mitral and tricuspid valves.
Arteriosclerosis, with extreme calcification of aorta and coronary arteries.
Chronic glomerulonephritis.
Adenocarcinoma of cecum.
Colloid adenoma of thyroid gland.
Reduplication cyst of duodenum.

Pathological Discussion

Dr. Mallory: We discovered a wide variety of anatomical findings, most of which Dr. Rawson has predicted correctly. There was a severe grade of heart disease, which was rather peculiar in character. As Dr. Lingley pointed out, in this x-ray film, there was an extreme grade of calcification of the annulus of the mitral valve, and almost equal calcification of the aortic ring. In neither valve was there any interadherence of the cusps or any shortening of the chordae tendineae, so that the gross picture was not characteristic of a chronic rheumatic endocarditis. There even was calcification of the annulus of the tricuspid, which is rare. Considerably to our surprise on microscopic examination the myocardium was full of fresh Aschoff bodies. We can say without doubt that the patient had a terminal acute rheumatic infection, since that is a pathognomonic lesion. There was a carcinoma of the cecum, which was ulcerated. The pressure defect on the duodenum was caused by a cyst, which I believe was congenital in origin, lying between the cecum and the gall bladder. It was lined with an enteric membrane and represented one of those reduplications of the intestinal tract often seen in children but rarely in adults. Evidently it had never caused any trouble.

Dr. Bauer: How large was it?

Dr. Mallory: About 4 or 5 cm. in diameter. There was also an extreme grade of arteriosclerosis in the entire aorta, as seen in the x-ray film. The aorta was calcified from the arch down to the iliac artery. There was likewise marked calcification in the coronary arteries. The thyroid gland showed only an old colloid adenoma. The kidneys were small, weighing 100 gm., and were finely granular and pale — the gross appearance usually associated with chronic glomerulonephritis. On microscopic section an active process was present. There had evidently been extensive destruction of the cortex, and we found an unusually marked sclerosis of the large and intermediate arteries, but little sclerosis of the arterioles, such as one sees in chronic nephrosclerosis. It seems astonishing to me that such a severe renal lesion had occurred without any record of hypertension. You may take your choice in attributing the anemia to the carcinoma or to the nephritis.

Dr. Rawson: The patient was in shock.

Dr. Mallory: But she had been under competent medical observation for three years and had never shown an elevated blood pressure in that period.

Dr. Rawson: Do you think that she had previously had early rheumatic lesions in the heart?

Dr. Mallory: I confess that I do not know how to interpret these calcareous lesions of the heart. The majority opinion is that they are rheumatic in origin. There has always been a small minority questioning that assumption, and I have been in the minority. In many of these cases the most frequent features of rheumatic involvement are missing. For example, in this case, there was no involvement of the valves and no thickening or shortening of the chordae, the two most reliable stigmas of old rheumatic involvement of the mitral valve. But I must grant the terminal rheumatic myocarditis.

CASE 32412

Presentation of Case

A forty-five-year-old screen painter entered the hospital because of swelling of the abdomen.

The patient had apparently been well until ten months before entry, when he became aware of increasing fatigue and exertional dyspnea. Five months later he noticed that he "looked thin" in the face and arms, and in another month a black bowel movement occurred. Six weeks before entry the abdomen gradually began to swell, and he caught a "cold," with a persistent hacking cough, occasionally productive of pinkish sputum. He also noticed that the stools were becoming light yellow and that his appetite was diminishing. Nevertheless he continued to work.

Twenty-five years before entry the patient had acquired a chancre on the penis, for which he received antisyphilitic therapy irregularly for the next twenty years. Fourteen years before entry, after a three-month period of treatment, he had become jaundiced but had recovered while still receiving intravenous injections. He admitted drinking two or three glasses of whisky a day for many years. For two years before entry he had had occasional epistaxes and bleeding gums, with some increase in bleeding tendency during the last two months before admission.

Physical examination revealed a poorly nourished man with a thin face and extremities and a protuberant abdomen. Numerous spider angiomas were scattered over the arms and back. There were dullness and a few medium rales at both lung bases. The heart was normal except for a faint, blowing systolic murmur heard best in the aortic area. The abdomen showed a prominent venous pattern and obvious ascites. The liver edge was felt two or three fingerbreadths below the costal margin. There were scattered hematomas over the legs but no ankle edema. The deep-tendon reflexes were normal.

The temperature, pulse and respirations were normal. The blood pressure was 132 systolic, 95 diastolic.

Examination of the blood showed a red-cell count of 4,400,000, with 75 per cent hemoglobin, and a white-cell count of 4700, with 63 per cent neutrophils and 30 per cent lymphocytes. The total protein was 7.8 gm. per 100 cc., with an albumin-globulin ratio of 0.56. The van den Bergh reaction was 1.0 mg. direct and 1.8 mg. total. The pro-

thrombin time was normal. The cholesterol was 327 mg. (normal, 150 to 230 mg.) and the phosphorus 3.3 mg. per 100 cc., the vitamin A 10 units (normal, 40 to 100 units) and the carotenoids 130 units per 100 cc. (normal, 100 to 300 units) and the alkaline phosphatase 9.1 Bodansky units. A cephalin-flocculation test was + in twenty-four hours and ++++ in forty-eight hours. Blood Hinton and Wassermann tests were positive. The urine was normal. A bromsulfalein test (5 mg. per kilogram of body weight) showed 36 per cent retention of the dye.

X-ray examination of the chest revealed several linear areas of segmented atelectasis in the left lower lung field and moderate collapse of the right middle lobe. The diaphragm showed adequate excursion, except for somewhat limited motion of the medial portion of the left dome. A gastrointestinal series disclosed extensive varicosities in the lower esophagus.

The patient was placed on a high-calorie, high-protein, high-vitamin, low-fat and low-salt diet, but no clinical improvement was noted. He complained of increased abdominal distention, as well as pain in the right chest posteriorly that was brought on by coughing or by raising the right arm. He also had several epistaxes. Mercupurin and ammonium chloride failed to control the ascites. On the tenth hospital day a paracentesis was performed, and 5500 cc. of straw-colored fluid removed. Repeated blood studies on the fifteenth hospital day revealed a total protein of 6.73 gm. per 100 cc., with an albumin-globulin ratio of 2.7. The van den Bergh reaction was 1.2 mg. direct and 1.4 mg. total. The prothrombin time was 25 seconds, with a normal control of 20 seconds. The cholesterol was 208 and the phosphorus 6.8 mg. per 100 cc., the vitamin A 50 and the carotenoids 40 units per 100 cc. and the alkaline phosphatase 6.8 Bodansky units. A cephalin-flocculation test was +++ in twenty-four hours and ++++ in forty-eight hours. The bleeding time was one and a half and the clotting time five minutes. On the twentieth hospital day the patient developed edema of the scrotum and prepuce. The radiosodium space was found to be 34 per cent of the body weight, and the thiocyanate space 43 per cent.*

On the twenty-second hospital day the patient began to vomit blood and passed grossly bloody stools. Gastrointestinal bleeding lasted for four days, and numerous blood transfusions were required to keep the patient out of shock. Four days later another 5700 cc. of abdominal fluid was removed, following which the patient appeared somewhat improved. A van den Bergh test was 3.2 mg. direct and 5.8 mg. total. On the thirty-third hospital day an x-ray film of the chest revealed a posterolateral fracture of the eighth rib that had not been seen previously. There were still areas of increased density in both lower lung fields. The ascites appeared to be forming more rapidly with each tap, and ankle edema was becoming noticeable. On the forty-first hospital day the blood phosphorus was 2.6 mg. per 100 cc., the alkaline phosphatase 10.0 Bodansky units and the total protein 6.77 gm. per 100 cc., with an albumin-globulin ratio of 0.5. The bromsulfalein test (2 mg. per kilogram of body weight) showed 95 per cent retention of the dye after thirty minutes. On the forty-third hospital day the patient again began to vomit blood, and on the following morning the temperature suddenly spiked to 105°F. The patient continued to vomit blood and to pass tarry stools. He went into shock and coma, but the systolic blood pressure returned to 150 after a transfusion. Nevertheless, the patient remained unresponsive, with the eyes half open and wandering from side to side and with the pupils rather large and responding to light. The legs and arms were extended and rigid, but the neck was not stiff. Arm and leg reflexes were hyperactive, and there was a positive Babinski sign on the right. The patient's condition remained unchanged, except that the arms gradually became flaccid. On the morning of the forty-fifth hospital day respirations became gasping and ceased.

*These measurements were carried out in the surgical research laboratories, where normal values for extracellular fluid volume average around 20 per cent of the body weight. Values over 33 per cent of the body weight are usually correlated with gross disturbances of electrolyte metabolism in which ions, normally extracellular in position, appear to move within the intracellular space. Values between 20 and 33 per cent of the body weight are associated with various grades of clinical edema. (Moore, F. D. Determination of total body water and solids with isotopes. *Science* **104**: 157-160, 1946.)

Differential Diagnosis

Dr. J. Wallace Zeller: The history is that of a patient with long-standing liver disease who developed rather rapidly progressive hepatic failure and portal obstruction. His death was preceded by bleeding from esophageal varices and possibly also by a terminal event involving the central nervous system.

The summary suggests that the patient had the hepatic facies. Ascites was obvious. A liver two or three fingerbreadths below the costal margin is probably enlarged if the upper level of dullness is in the fifth intercostal space. Apparently the liver was not noted to be definitely nodular. The spleen was not commented on, so that it may be assumed that it was not felt.

The low white-cell count and the alterations in the serum protein are frequently found in severe liver disease. No comment concerning jaundice is made, although the van den Bergh reaction rose to a total of 5.8 mg. At that level clinical jaundice is usually evident. The epistaxes and hematomas of the lower legs are probably related to the prolonged prothrombin time and the alteration in vitamin K metabolism associated with severe liver disease. The results of the bromsulfalein tests reveal marked hepatic insufficiency. The elevation in serum cholesterol, the low serum vitamin A level,

the elevated alkaline phosphatase and the abnormal cephalin-flocculation tests are all changes that might be expected in diffuse liver disease.

The record gives no history of definite injury, which may have been a cause for the fracture of the eighth rib. The fracture was present on the right side and may well have caused the pain in the right posterior chest that was brought on by coughing and raising the right arm. This lesion of course may have been a cough fracture, since we are informed that a persistent hacking cough was present for six weeks before entry. This was most probably due to bronchitis. The areas of atelectasis and collapse that developed may have been due to collections of mucus in the bronchi and small bronchial radicles.

The combination of hepatic failure and portal obstruction naturally brings cirrhosis of the liver to the fore as the likeliest diagnostic possibility. In explaining the etiology of such a lesion we are given at least three possibilities by the history. These are in the order of likelihood: alcohol, syphilis and arsenical antisyphilitic therapy. I believe that we may assume that the intravenous injections the patient was receiving when he became jaundiced were arsphenamine or neoarsphenamine. The fact that the jaundice disappeared while the injections were continued makes it unlikely that he had a true arsenical hepatitis. It should be stated that the continuance of arsenical therapy in the presence of jaundice is fearless but unjustified treatment for syphilis. There is a good possibility of producing acute yellow atrophy by such means. The cirrhosis that develops following injury to the liver from arsenic is not true portal cirrhosis. Syphilis itself can cause cirrhosis of the portal type. This patient's syphilitic infection was irregularly, and therefore inadequately, treated. The history and findings are consistent in every way with a diagnosis of alcoholic cirrhosis of the liver. The possibility that alcohol and one or more of the other two factors were simultaneously involved must be considered.

An additional etiologic factor that sometimes causes jaundice in patients receiving arsenical antisyphilitic treatment is epidemic infectious hepatitis. Cases in which this has been traced in clinics to improperly cleaned needles and syringes have been reported. In this regard it is of interest to note that studies of liver biopsies of patients with epidemic infectious hepatitis, arsenical hepatitis and homologous serum jaundice reveal no definite histologic differences in the three conditions.

The gastrointestinal bleeding, which was a prominent feature of the terminal course, undoubtedly had its origin in the esophageal varices. The increased van den Bergh reaction noted at that time may have been partially due to the absorption of blood pigment from the intestine.

During the last day of life the patient was in coma. Various transient paralyses may occur in so-called "hepatic coma." The changes described could have been due to a left-sided cerebral hemorrhage, possibly associated with the rupture of a syphilitic aneurysm. The extension and rigidity of the extremities could be interpreted as a manifestation of cerebral irritation preceding the stage of paralysis and flaccidity. It is entirely possible that these terminal manifestations could occur without bleeding into the brain, however.

There is good evidence from the history and serologic reactions that this patient had syphilis. Aside from a possible syphilitic factor as a contributing cause of the liver disease and the less likely presence of a syphilitic cerebral aneurysm, there is little evidence from this record of syphilis of other organs. That does not mean, of course, that it will not be found.

My final diagnosis is portal cirrhosis of the liver, with bleeding esophageal varices, ascites and final hepatic failure. It is entirely possible that some fresh destructive lesions of the liver cells will be found, in addition to the old cirrhosis. Alcohol and possibly syphilis are the likeliest etiologic factors to be associated with the cirrhosis. Arsphenamine or infectious hepatitis may have played a contributing role, although they are not usually considered causes of typical portal cirrhosis.

Clinical Diagnoses

Cirrhosis of liver, ? type.
Cerebral hemorrhage or thrombosis.

Dr. Zeller's Diagnoses

Portal cirrhosis of liver.
Bleeding esophageal varices.
Ascites.
Hepatic failure.

Anatomical Diagnoses

Hepatoma, with portal vein invasion and thrombosis.
Cirrhosis of liver, alcoholic type.
Esophageal varices, with massive hemorrhage.
Ascites.
Necrotizing bronchopneumonia.
Fibrous pleuritis.
Arteriosclerosis, generalized and coronary.
Healing fractures, right seventh and eighth ribs.

Pathological Discussion

Dr. Tracy B. Mallory: This patient showed, as Dr. Zeller predicted, a severe cirrhosis of the liver, with esophageal varices from which the numerous attacks of bleeding had come. There was, however, something more. The liver was significantly enlarged, weighing over 2200 gm., and the surface showed a combination of coarse nodularity and fine granulation. On section it was obvious that a large part of the liver had been replaced by tumor, which was spreading in the form of thrombi throughout the intrahepatic portal vein. The thrombus ex-

tended back about 1 cm. in the portal vein beyond its point of exit from the liver substance. The identifiable hepatic veins were free from tumor. It is somewhat more usual to find invasion of the hepatic rather than the portal vein. The process was so extensive in this case that the portal obstruction must have been complete. On microscopic examination the tumor proved to be a characteristic hepatoma, with an excellent grade of differentiation, leaving no room for doubt regarding the diagnosis. In the portion of the liver not invaded by tumor a finely granular cirrhosis was present. There were many foci of fresh infarct-like necrosis, presumably due to the venous obstruction. Too little of the cirrhotic portion was uninvolved to permit a definite opinion concerning the type of cirrhosis; it was quite compatible with an alcoholic type. Dr. Zeller avoided the trap of assuming that the rib fracture, without a clear history of trauma, was a pathologic fracture due to metastases. Section through the area of fracture showed active bone callus but no evidence of tumor.

Despite the profound central-nervous-system symptoms the brain showed relatively little. There were no gross areas of hemorrhage or softening, and the arterial system showed no point of occlusion. There was a slight granularity of the ependyma, and a few perivascular foci of lymphocytes could be found. These are compatible with a low grade of central-nervous-system syphilis, and it is doubtful if they were connected in any way with the hepatic insufficiency. Experience with the fulminating type of hepatitis during the war made many of us familiar with the marked central-nervous-system symptoms that may accompany hepatic insufficiency. I saw a few patients with hepatitis who died so rapidly that jaundice never developed. In these patients the central-nervous-system symptoms completely dominated the clinical picture. The anatomic findings in the brain were always disappointing. Slight clouding of the meninges and occasional foci of perivascular cuffing were all that was ever seen. The situation is analogous to that in uremia, in which, again, prominent central-nervous-system symptoms are present but minimal nonspecific lesions can be found only in the brain.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

WORLD HUNGER

Despite the inevitable association between war and famine, when the ploughshare is beaten into a sword and the farmer must leave his field to wield the sword, the present world famine goes deeper even than the recent world war. Ploughed fields, it is true, have been trampled into mud by the hurrying feet of the world's greatest armies and torn asunder by the destructiveness of their machines, but Nature has also set the stage for her own act in this common disaster.

Over two years ago, in the summer of the Southern Hemisphere, according to a recent issue of *Future*, Latin America was visited with its worst drought in eighty-six years. Argentina's wheat production fell to 60 per cent of normal, and her corn crop to a third, while Cuba's sugar crop practically dried up at the source. At the same time a drought affected North Africa, breadbasket of France and the Mediteranean basin, so that by the end of 1945 the grain output of this region had dropped from four million to scarcely one million tons. Half the wheat crop and most of the potatoes and beans were failing in South Africa, and this section had to import food by the end of 1945; Australia went dry, and the worst drought in modern times, following heavy rains, destroyed the 1945 crops of the Danube basin. This drought also visited Italy, Spain, France and the Low Countries. Finally the rains have failed in India, Ceylon and Burma, the last-named country being the world's largest exporter of rice. In addition, rinderpest has struck Burma's work cattle, killing a large proportion of them. This year Burma will have no rice to export.

Apparently only the United States, Canada, part of the Middle East and perhaps imponderable Russia are continuing to raise bumper crops, and they must tide over the rest of the world until it can again begin to feed itself. Mass starvation, it is said, has been averted for the time being, but mass malnutrition is dangerously close to the line, and this will prevail at least until the 1947 crops are harvested.

The Department of Agriculture announced in June the failure of this country to meet its export goal of grain and fats and oils for the first quarter of the year; the report of the Secretary of Agriculture to the President on July 8 announced that the fiscal year's grain commitment of 400 million bushels had been met by June 30. This shipment, moreover, was nearly double the requirement for the year that was presented to the Combined Food Board a year ago. Figures, particularly astronomical figures, have little meaning for the individual, impressive as they may appear. Thus, it means little to learn that we have exported, during the fiscal year, 16,700,000 long tons of food unless we know what relation this bears to our normal exports, to our total production, to the exports of other food-producing countries and, particularly, to the world's present needs.

We are passing through an unprecedented period of famine. Are we doing our share in its control, and how successful can we expect its control to be?

COMBINED SULFONAMIDE AND PENICILLIN THERAPY

THE desirability of using both sulfonamides and penicillin in the treatment of infections that are susceptible to both agents is a practical everyday problem. It is amenable, in part, to study in the test tube and in experimental infections of animals, but the final answer must come from a careful analysis of many factors and particularly from the results of clinical experience.

Most but not all of the experimental evidence suggests that the combined use of both agents is preferable to the use of either one alone. Ungar[1] reported that sulfapyridine has a synergistic effect on the action of penicillin against *Staphylococcus aureus* and *Streptococcus haemolyticus* in vitro and in mice. Bigger[2, 3] found that sulfathiazole increases the dilution in which the inhibitory action of penicillin takes place. He therefore advocated the combined use of the two agents in staphylococcal infections and suggested that the combination might even prove effective against the typhoid bacillus. Kirby[4] also demonstrated that urea-penicillin and sulfonamide-penicillin mixtures produce greater bacteriostasis of cultures of staphyloccoci than does penicillin alone. This, however, he found to be purely an additive effect and not a potentiation, since the combination was not inhibitory in concentrations that did not inhibit separately.

The differences in the mode of action of the sulfonamides and of penicillin should be borne in mind. Hobby and Dawson[5] found that penicillin is most effective during the active multiplication of bacteria and that the concentration of the organisms, within fairly wide limits, is not important so long as multiplication occurs and a sufficient concentration of penicillin is present. The sulfonamides, on the other hand, they[6] found to be effective only after a lag period during which the organisms multiply while in contact with the drug. Sulfonamides added after organisms had passed the growth acceleration phase produced no bacteriostasis. In addition, the sulfonamides did not act on large numbers of organisms even if they were actively multiplying. They concluded that there was no evidence of any synergistic action of sulfonamides on penicillin. They also thought that para-aminobenzoic acid did not increase the effective titer of penicillin but did increase its rate of action, presumably under conditions in which it enhances growth.

More detailed studies by Hobby and Dawson[7] showed that the results obtained with the combined use of penicillin and sulfadiazine are dependent on many factors. Among these are the concentration of each bacteriostatic agent, the number of organisms present, the environmental conditions allowing growth of the organisms, the susceptibility of the organism to the two agents and the organisms involved.

When penicillin was present in amounts so small as to produce little or no bacteriostasis, sulfadiazine increased the bacteriostatic action provided that the organism was sensitive to the sulfonamide and was present in small numbers. In the presence of an amount of penicillin that by itself was sufficient to produce a definite bacteriostatic or bactericidal effect during the first few hours of incubation but insufficient to yield complete sterilization, sulfadiazine increased bacteriostasis; but again, this occurred only when the number or organisms at the end of the sulfadiazine lag was low. Hobby and Dawson thought that the sensitivity of the organism to sulfadiazine enhanced this effect, but that the degree of sensitivity did not necessarily have to be sufficient to be demonstrable by the usual methods.

With larger amounts of penicillin, its bactericidal action was rapid during the first few hours of incubation and complete sterilization often resulted within five to seven hours. If sterilization was not complete at the end of that time, the presence of sulfadiazine sometimes actually prolonged the lag period or even slightly decreased the bactericidal rate. It appears, therefore, that since the action of penicillin occurs predominantly at the time of cell division, a decrease in the rate of multiplication due to sulfadiazine can decrease the rate at which penicillin acts.

The results of similar studies were briefly reported by Vigouroux and Leyton.[8] They found that the antibiotic action of penicillin for a number of strains of pathogenic bacteria was reinforced over a wide range by the addition of small amounts of either sulfathiazole, sulfapyridine, sulfadiazine or para-

aminobenzoic acid. The incorporation of one of the sulfonamides and para-aminobenzoic acid in the same solution with penicillin nullified the potentiation. A penicillin-para-aminobenzoic acid mixture had a more pronounced action on penicillin-sensitive strains, however, than did a combination of penicillin and one of the sulfonamides. The sensitivity of the organism to penicillin played no part in the latter potentiation but, according to these workers, was related to the intrinsic antibacterial action of the substance under investigation. Occasional organisms were encountered that were susceptible to penicillin-sulfonamide mixtures but resistant to each agent applied separately. On the basis of their results, these authors thought that the combination of sulfonamides and penicillin is indicated in certain infections.

There are clinical conditions in which sulfonamides have been found empirically to add to the effect of penicillin. This is particularly true in cases of meningitis due to organisms that are susceptible to both agents. In such cases the mortality obtained with the combined use of sulfonamides and penicillin, the latter given both intrathecally and intramuscularly, is lower than that obtained with either antibacterial agent used alone. Probably similar results may be expected in other bacterial infections in which there is a tendency of the infection to focalize in inaccessible areas. In such conditions the problems of penetration and diffusion into the infected foci may be an important factor. Differences in the susceptibility of the organisms and the possible additive effect of the two agents, however, may also be significant.

Evidence suggesting that penicillin diffuses into fibrin clots whereas sulfonamides do not[9] may help to explain the better results obtained with the former in cases of bacterial endocarditis and possibly also in some cases of empyema. The failure of penicillin to penetrate in adequate amounts into the cerebrospinal fluid after systemic administration and probably also the greater susceptibility of the bacterial strains to sulfonamides may account for the better results obtained with sulfadiazine in cases of meningococcal meningitis. Combined therapy has not usually proved advantageous in these circumstances.

In the last analysis, the question of the clinical use of combined penicillin and sulfonamides must be considered as a problem to be decided according to the particular circumstances of any given case. Among other factors one must take into account the desirability of giving frequent injections of penicillin or of subjecting the patient to the possible toxic effects of the sulfonamides. A large increase in the dosage of penicillin is usually more effective than the additional use of sulfonamides. Combined therapy is usually reserved for the severest cases and seems to produce the best results in such cases. This has recently been shown to be true in pneumonia[10] as well as in meningitis.

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KILLAM, ARTHUR R., 1 Parker Road, Winchester.
Boston University School of Medicine, 1944.

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CARP, JACOB S., 206 Elliot Street, Newton Upper Falls.
Middlesex University School of Medicine, 1940. Sponsor: Israel Kahalas, Newton; office, 483 Beacon Street, Boston

DENNEHY, TIMOTHY J., 106 Algonquin Road, Chestnut Hill.
Georgetown University School of Medicine, 1944.

ETTENBERG, MAX, 120 White Street, Belmont.
Middlesex University School of Medicine, 1940. Sponsor: Samuel E. Chalfen, 50 Follen Street, Cambridge.

FEINGOLD, MYER, 584 Salem Street, Malden.
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GLICKLICH, EARL A., 81 Undine Road, Brighton.
University of Cincinnati College of Medicine, 1938.

GOLDBERG, M. Milton, Malden Hospital, Malden.
Tufts College Medical School, 1940.

GORFINE, MORRIS, 144 Jaques Street, Somerville.
Middlesex University School of Medicine, 1938. Sponsor: Robert Gorfine, 120 Brainerd Road, Allston.

GRODEN, HAROLD M., 1531 Cambridge Street, Cambridge.
Tufts College Medical School, 1939.

HIRSCH, LAWRENCE S., 42 Lincoln Street, Framingham.
Middlesex University School of Medicine, 1940. Sponsor: Frederick H. Salls, 132 Union Avenue, Framingham.

HOFFMAN, JOHN L., 7 Arlington Street, Cambridge.
University of Buffalo School of Medicine, 1924.

LEVENSON, HERBERT M., 141 Sutherland Road, Brighton.
Boston University School of Medicine, 1940.

LEVINSON, LEON, 40 Cloverdale Road, Newton Highlands.
Tufts College Medical School, 1943.

LEVREAULT, GERALD V., 26 Chase Street, Newton Centre.
Tufts College Medical School, 1942.

MCARTHUR, JANET W., 204 Pleasant Street, Arlington.
Northwestern University Medical School, 1942.

MONAGHAN, LEO B., Old Road to Nine Acre Corner, Concord.
Tufts College Medical School, 1943.

MOSHER, HENRY A., 11 Beatrice Circle, Belmont.
Northwestern University Medical School, 1938.

O'HARA, JOHN L., 136 Hunnewell Avenue, Newton.
Tufts College Medical School, 1941.

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Harvard Medical School, 1942.

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Middlesex University School of Medicine, 1937. Sponsor: Burton C. Grodberg, 640 Main Street, Malden.

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SCARINGI, JOSEPH, 66 Curtis Street, West Somerville.
Middlesex University School of Medicine, 1937. Sponsor: Edmund H. Robbins, 334 Broadway, Somerville.

SHARRY, CHARLES F., 5-A Bigelow Street, Cambridge.
Harvard Medical School, 1915.

SOMMERS, SHELDON C., 57 Kenwood Avenue, Newton Centre.
Harvard Medical School, 1941.

STEIMAN, SOLOMON E., 1874 Commonwealth Avenue, Brighton.
Boston University School of Medicine, 1943.

SWANK, ROY L., 105 Wood End Road, Newton Highlands.
Northwestern University Medical School, 1935.

TIERNEY, THOMAS M., 1980 Commonwealth Avenue, Brighton.
Georgetown University School of Medicine, 1942.

TRODELLA, GEORGE P., 95 Pearl Street, Somerville.
Tufts College Medical School, 1943.

TULLIS, JAMES L., 9 Billings Park, Newton.
Duke University School of Medicine, 1940.

WARREN, KENNETH W., 1371 Walnut Street, Newton Highlands.
Temple University School of Medicine, 1938.

WILHELM, NORBERT A., 160 Lake Avenue, Newton Centre.
St. Louis University School of Medicine, 1925.

WILLIAMS, NATHAN, 264 Kelton Street, Allston.
Boston University School of Medicine, 1939.

WOODS, FRANCIS M., 60 Brush Hill Road, Newton Highlands.
Yale University School of Medicine, 1933.

WORCESTER, JOHN, 87 Allen Avenue, Waban.
Tufts College Medical School, 1939.

WYMAN, STANLEY M., 840 Massachusetts Avenue, Arlington.
Harvard Medical School, 1939.

YORK, RICHARD F., 918 Chestnut Street, Waban.
Middlesex University School of Medicine, 1940. Sponsor: Laurence J. Louis, 1515 Centre Street, Newton Centre.

Alexander A. Levi, *Secretary*
481 Beacon Street, Boston

NORFOLK DISTRICT

ALEXANDER, EBEN, JR., 27 Longwood Avenue, Brookline.
Harvard Medical School, 1939.

ALFORD, HYMAN, 4 Thane Street, Dorchester.
Tufts College Medical School, 1941.

BARTOL, GEORGE M., 126 Woodlawn Avenue, Wellesley Hills.
University of Pennsylvania School of Medicine, 1939.

BLUESTEIN, LOUIS L., 60 Lincoln Street, Hyde Park.
Middlesex University School of Medicine, 1941. Sponsor: Charles Korb, 1259 Hyde Park Avenue, Hyde Park.

BRAGDON, JOSEPH H., 93 Common Street, Dedham.
Columbia University College of Physicians and Surgeons, 1939.

BROOKS, EUGENE F., Wrentham.
Middlesex University School of Medicine, 1939. Sponsor: Karl V. Quinn, Wrentham State School, Wrentham.

BROWN, FRANCIS H., 31 Monadnock Road, Wellesley Hills.
Tufts College Medical School, 1941.

CARROLL, JOHN J., 107 Harvard Street, Dedham.
Tufts College Medical School, 1931.

CHAPMAN, CARLETON B., 295 Walnut Street, Brookline.
Harvard Medical School, 1941.

CLINTON, MARSHALL, JR., 324 Linden Street, Wellesley.
University of Buffalo School of Medicine, 1940.

COBURN, MORTON B., 48 Browne Street, Brookline.
Middlesex University School of Medicine, 1939. Sponsor: Benjamin F. Sieve, 134 Sewall Avenue, Brookline.

COHEN, SIDNEY, 214 Riverway, Boston.
Harvard Medical School, 1937.

COLEMAN, NATHAN W., 38 Greendale Road, Mattapan.
Middlesex University School of Medicine, 1941. Sponsor: Eli Friedman, Roxbury; office, 416 Marlboro Street, Boston.

COX, GEORGE E., 38 Highland Street, Hyde Park.
Middlesex University School of Medicine, 1935. Sponsor: Irving J. Shalett, 1589 Beacon Street, Brookline.

CURLEY, GEORGE A., 853 Cummins Highway, Mattapan.
College of Physicians and Surgeons, Boston, 1937. Sponsor: Henry L. Pelkus, 15 Fairmount Avenue, Hyde Park.

ECHLOV, THEODORE G., 112 Salisbury Road, Brookline.
Middlesex University School of Medicine, 1940. Sponsor: William Dameshek, Brookline; office, 192 Beacon Street, Boston.

EHRENBERG, RUTH, Boston State Hospital, Dorchester.
University of Berlin, 1926. Sponsor: Walter E. Barton, Boston State Hospital, Dorchester.

EMERSON, KENDALL, JR., 71 Griggs Road, Brookline.
Harvard Medical School, 1933.

ENGLAND, ALBERT C., JR., 42 Griggs Terrace, Brookline.
Harvard Medical School, 1937.

FOX, HENRY M., 17 Clark Road, Wellesley Hills.
Johns Hopkins University School of Medicine, 1933.

FRECHETTE, ALFRED L., 673 High Street, Westwood.
University of Vermont College of Medicine, 1934.

GOLDBERG, IRVING E., 103 Winthrop Street, Roxbury.
Medical College of the State of South Carolina, 1940.

HASTINGS, NELSON, 70 Cypress Street, Brookline.
Harvard Medical School, 1940.

HAYDEN, CHARLES G., 59 Vernon Street, Brookline.
University of Minnesota Medical School, 1941.

HERMANSON, ROBERT H., 268 Mason Terrace, Brookline.
Tufts College Medical School, 1939.

KALDECK, RUDOLPH, 591 Morton Street, Dorchester.
University of Vienna, 1912. Sponsor: Walter E. Barton, Boston State Hospital, Dorchester.

KARRAS, JOSEPH D., 82 Stedman Street, Brookline.
Middlesex University School of Medicine, 1937. Sponsor: George A. Small, 81 Walpole Street, Norwood.

KELLEY, THOMAS F., 384 Boylston Street, Brookline.
Boston University School of Medicine, 1939.

KICKHAM, EDWARD F., 657 Chestnut Hill Avenue, Brookline.
Tufts College Medical School, 1941.

LARCOM, RODNEY C., JR., 481 Washington Street, Dedham.
Harvard Medical School, 1940.

LAYTON, MANUEL L., 50 Winston Road, Dorchester.
Middlesex University School of Medicine, 1932. Sponsor: Jacob Applebaum, 371 Commonwealth Avenue, Boston.

LENSON, NORMAN, 55 Wilcox Street, Dorchester.
Tufts College Medical School, 1943.

LEVINE, ALBERT, 939 Morton Street, Mattapan.
Middlesex University School of Medicine, 1937. Sponsor: Samuel L. Marnoy, Brookline; office, 311 Commonwealth Avenue, Boston.

LEWENSTEIN, HOWARD J., 9 Leland Road, Brookline.
Tufts College Medical School, 1942.

LEWIS, ROGER A., 38 Kilsyth Road, Brookline.
Johns Hopkins University School of Medicine, 1938.

LOTH, ERIC C., 28 Montebello Road, Jamaica Plain.
Middlesex University School of Medicine, 1939. Sponsor: Arnold N. Allen, 961 South Street, Roslindale.

LYNCH, ALICE D., 28 Bellevue Street, Dorchester.
Tufts College Medical School, 1930.

MALOOF, EMIL G., 3 New Park Avenue, West Roxbury.
Middlesex University School of Medicine, 1936. Sponsor: Antonio P. Milone, 4354 Washington Street, Roslindale.

MCCOMBS, ROBERT P., 1514 Beacon Street, Brookline.
University of Pennsylvania School of Medicine, 1935.

MCNAMARA, THOMAS J., 58 St. Rose Street, Jamaica Plain.
Tufts College Medical School, 1942.

MELINE, DAVID I., 72 Maywood Street, Roxbury.
Middlesex University School of Medicine, 1937. Sponsor: Benjamin F. Bornstein, Chestnut Hill; office, 370 Commonwealth Avenue, Boston.

MORRISON, HERBERT S., 89 Englewood Avenue, Brookline.
McGill University Faculty of Medicine, 1945.

MORSE, LAWRENCE S., 73 Thatcher Street, Brookline.
Tufts College Medical School, 1938.

O'Brien, Joseph A., 11 Shenandoah Street, Dorchester. Tufts College Medical School, 1941.

O'Brien, Paul I., 102 Wheatland Avenue, Dorchester. Tufts College Medical School, 1942.

O'Connell, William T., 40 Murray Hill Road, Roslindale. Tufts College Medical School, 1943.

Park, Irving H., 64A University Road, Brookline. Middlesex University School of Medicine, 1937. Sponsor: Thomas P. Kendrick, 454 Washington Street, Brookline.

Pier, Arthur S., Jr., 539 Brush Hill Road, Milton. Harvard Medical School, 1939.

Pilka, Dominic, 40 Mill Street, Dorchester. Middlesex University School of Medicine, 1929. Sponsor: Paul J. Jakmauh, Milton; office, 509 Broadway, South Boston.

Powers, Hazel C. Kanz, 74 Fenwood Road, Boston. Middlesex University School of Medicine, 1924. Sponsor: Elizabeth Z. Kleinman, 66 Perkins Street, Jamaica Plain.

Powers, Joseph W., 121 Blue Hill Avenue, Roxbury. Kansas City University of Physicians and Surgeons, 1937. Sponsor: Bernard A. Godvin, Jamaica Plain; office, 483 Beacon Street, Boston.

Putnam, Henry M., 151 Grove Street, Westwood. Harvard Medical School, 1935.

Rand, Harry, 16 Baird Street, Dorchester. Middlesex University School of Medicine, 1935. Sponsor: Charles Silverstein, 99 Stratton Street, Dorchester.

Roodin, Harry, 100 Seaver Street, Roxbury. College of Physicians and Surgeons, Boston, 1940. Sponsor: Moses J. Stone, West Roxbury; office, 520 Beacon Street, Boston.

Rosen, Daniel, 66 Columbia Road, Roxbury. University of Vienna, 1936. Sponsor: Hyman B. Goldberg, 2 Pasadena Road, Dorchester.

Rosmartin, Ernest, 14 Autumn Street, Boston. University of Vienna, 1906. Sponsor: Hyman Morrison, Brookline; office, 483 Beacon Street, Boston.

Shapiro, Eli, 484 Blue Hill Avenue, Roxbury. Middlesex University School of Medicine, 1937. Sponsor: George Robbins, Brookline; office, 416 Marlboro Street, Boston.

Swartz, Morris, 22 Wentworth Terrace, Dorchester. Boston University School of Medicine, 1935.

Tribby, William W., 198 Aspinwall Avenue, Brookline. Harvard Medical School, 1937.

Welch, C. Stuart, 170 Dudley Street, Brookline. Tufts College Medical School, 1932.

Wise, H. Robert, 36 Schuyler Street, Roxbury. Middlesex University School of Medicine, 1936. Sponsor: Nicholas J. King, 43 Cummins Highway, Roslindale.

Zindwer, Renee, 4076 Washington Street, Roslindale. University of Vienna, 1938. Sponsor: Marjorie Woodman, Jamaica Plain; office, 21 Bay State Road, Boston.

Basil E. Barton, *Secretary*
10 Richwood Street, West Roxbury

Norfolk South District

Amerena, John P., 230 North Main Street, Randolph. Middlesex University School of Medicine, 1937. Sponsor: Edmund B. FitzGerald, 563 Furnace Brook Parkway, Quincy.

Ballin, Ludwig, Norfolk County Hospital, South Braintree. University of Munich, 1924. Sponsor: Nahum R. Pillsbury, Norfolk County Hospital, South Braintree.

Collins, Gerald M., 4 High Street, Hingham. Boston University School of Medicine, 1941.

Hecht, Paul L., 428 Washington Street, Braintree. University of Freiburg, 1920. Sponsor: Clifford F. Danforth, 165 Washington Street, Weymouth.

Millen, Morris H., 391 Bridge Street, North Weymouth. Middlesex University School of Medicine, 1933. Sponsor: William S. Altman, 32 Spear Street, Quincy.

Nevins, Simon H., 611 Adams Street, Quincy. Middlesex University School of Medicine, 1925. Sponsor: Harry Braverman, 43 School Street, Quincy.

Sloane, William C., 15 South Main Street, Randolph. Middlesex University School of Medicine, 1933. Sponsor: Frank W. Crawford, 98 North Franklin Street, Holbrook.

Ebenezer K. Jenkins, *Secretary*
Norfolk County Hospital, South Braintree

Plymouth District

Arnone, William H., 147 Myrtle Street, Brockton. New York University College of Medicine, 1942.

Carpinella, Charles J., 94 Moraine Street, Brockton. Middlesex University School of Medicine, 1931. Sponsor: Victor V. Ragonetti, 145 Court Street, Plymouth.

DeSimone, John S., 145 West Elm Street, Brockton. Middlesex University School of Medicine, 1939. Sponsor: John A. Carriuolo, 290 Forest Avenue, Brockton.

Donnelly, James F., 63 Franklin Avenue, Rockland. Middlesex University School of Medicine, 1939. Sponsor: Joseph H. Dunn, 321 Union Street, Rockland.

Enos, Allen W., Broadway, Hanover. Middlesex University School of Medicine, 1939. Sponsor: Joseph H. Dunn, 321 Union Street, Rockland.

Mayo, Walter V., 119 Summer Street, Kingston. Middlesex University School of Medicine, 1936. Sponsor: George A. Moore, 167 Newbury Street, Brockton.

McCluskey, John E., 932 Main Street, Brockton. Middlesex University School of Medicine, 1940. Sponsor: Joseph S. Phaneuf, 688 North Main Street, Brockton.

Moore, Kenneth T., Washington Street, Hanover. Hahnemann Medical College, 1936.

Putnam, Robert M., 31 North Street, Plymouth. McGill University Faculty of Medicine, 1944.

Sheehan, John C., Marginal Street, Green Harbor. Tufts College Medical School, 1943.

Weiss, Samuel, 47 West Elm Street, Brockton. Tufts College Medical School, 1930.

Ralph C. McLeod, *Secretary*
Goddard Hospital, Brockton

Suffolk District

Albert, Harold S., 476 Beacon Street, Boston. McGill University Faculty of Medicine, 1943.

Cannon, Raymond G., 158 O Street, South Boston. Middlesex University School of Medicine, 1940. Sponsor: John J. Todd, 587 Beacon Street, Boston.

Capodilupo, Graziano A., 109 Prince Street, Boston. Middlesex University School of Medicine, 1935. Sponsor: Anthony O. Cardullo, 261 Hanover Street, Boston.

Carter, Barbara F., 256 Beacon Street, Boston. Tufts College Medical School, 1942.

Ford, Richard, 157 Newbury Street, Boston. Harvard Medical School, 1940.

Golden, Isaac, 174 Chestnut Street, Chelsea. Middlesex University School of Medicine, 1936. Sponsor: Benjamin I. Cassin, 195 Chestnut Street, Chelsea.

Guarciariello, Cosmo A., 131 Endicott Street, Boston. Royal University of Rome, 1935. Sponsor: E. Parker Hayden, 270 Commonwealth Avenue, Boston.

Harris, Oliver J., 334 Beacon Street, Boston. Tufts College Medical School, 1940.

Helman, Milton E., 18 Lynn Street, Chelsea. Boston University School of Medicine, 1940.

Hinton, Elmer E., 386 Commonwealth Avenue, Boston. University of Kansas School of Medicine, 1941.

Kennan, Fred J., 1 James Street, Boston. Tufts College Medical School, 1935.

King, Myron N., 132 Shore Drive, Winthrop. University of Vermont College of Medicine, 1941.

Luongo, Angelo J., 17 Vinal Street, Revere. Middlesex University School of Medicine, 1934. Sponsor: Harold L. Musgrave, 620 Beach Street, Revere.

McKeigue, John E., 3 Poplar Place, Boston.
Jefferson Medical College of Philadelphia, 1942.

Miller, Harold, 48 Addison Street, Chelsea.
Midwest Medical College, 1937. Sponsor: Aubrey C. Benjamin, 35 Eleanor Street, Chelsea.

Myerson, Paul G., 66 Fenway, Boston.
Harvard Medical School, 1939.

Paull, Thomas, Boston City Hospital, Boston.
Harvard Medical School, 1940.

Pipi, John, 821 Saratoga Street, East Boston.
Middlesex University School of Medicine, 1935. Sponsor: Pasquale Costanza, 238 Maverick Street, East Boston.

Prescott, Blake D., 41 Deerfield Road, Wethersfield, Conn.
Middlesex University School of Medicine, 1931. Sponsor: Davis T. Gallison, 520 Commonwealth Avenue, Boston.

Record, Eugene E., 308 Commonwealth Avenue, Boston.
McGill University Faculty of Medicine, 1937.

Ripa, Anthony S., 523 Beacon Street, Boston.
Middlesex University School of Medicine, 1936. Sponsor: Louis Cohen, 108 Meridian Street, East Boston.

Rupp, John J., 39 North Russell Street, Boston.
Washington University School of Medicine, 1944.

Viterbi, Achille, 250 Commonwealth Avenue, Boston.
University of Turin, 1905. Sponsor: Carl F. Maraldi, 276 Commonwealth Avenue, Boston.

Weinberger, Jerome L., 117 Bay State Road, Boston.
New York University College of Medicine, 1938.

Wolfe, Louis M., 11 Lawrence Street, Chelsea.
New York University College of Medicine, 1939.

Robert L. Goodale, *Secretary*
330 Dartmouth Street, Boston

Worcester District

Adams, Lambi N., St. Vincent's Hospital, Worcester.
Hahnemann Medical College, 1941.

Benoit, Noe N., 17 Grove Street, Millbury.
Tufts College Medical School, 1942.

Brown, Chester W., 32 Buckley Road, Worcester.
University of Rochester School of Medicine, 1939.

Deering, George E., Jr., 299 Belmont Street, Worcester.
Harvard Medical School, 1943.

Gould, Maxwell E., 20 Goldthwait Road, Worcester.
Middlesex University School of Medicine, 1938. Sponsor: Ralph S. Perkins, 27 Elm Street, Worcester.

Guild, S. Alden, 15 Worcester Street, Grafton.
Tufts College Medical School, 1942.

Jewett, Everett P., 2 Bellingham Road, Worcester.
Tufts College Medical School, 1943.

Karpawich, Peter P., 237 Millbury Street, Worcester.
Hahnemann Medical College, 1940.

Kuekan, James R., 54 Cottage Street, Whitinsville.
Tufts College Medical School, 1944.

Lareau, Henry R., 62 Mechanic Street, Spencer.
Boston University School of Medicine, 1942.

LaVigne, Richard J., 467 Chandler Street, Worcester.
Tufts College Medical School, 1941.

Lavoie, Robert J., 170 Dana Avenue, Worcester.
Hahnemann Medical College, 1941.

Pellock, Charles J., 515 Main Street, Shrewsbury.
College of Physicians and Surgeons, Boston, 1936. Sponsor: Edward O. Horne, 24 Holman Street, Shrewsbury.

Scricco, Michael W., 13 Shelby Street, Worcester.
Albany Medical College, 1941.

Seidenberg, Daniel, 845 Main Street, Worcester.
Kansas City University of Physicians and Surgeons, 1929. Sponsor: Oscar Feinsilver, 390 Main Street, Worcester.

Shannon, Mary C., 334 Highland Street, Worcester.
Kansas City University of Physicians and Surgeons, 1927. Sponsor: Ernest L. Hunt, 28 Pleasant Street, Worcester.

Sikorsky, Lucy N., 4 Oak Street, Grafton.
Boston University School of Medicine, 1928.

Starr, Steven J., St. Vincent's Hospital, Worcester.
Georgetown University School of Medicine, 1941.

Wojciechowski, Anthony A., 38 Crosby Street, Webster.
Tufts College Medical School, 1942.

Julius J. Tegelberg, *Secretary*
57 Cedar Street, Worcester 2

Worcester North District

Lamb, Marshall A., 197 Central Street, Winchendon.
Tufts College Medical School, 1939.

Rittenhouse, Harvey L., 20 Pleasant Street, Ayer.
College of Medical Evangelists, 1943.

James G. Simmons, *Secretary*
30 Myrtle Avenue, Fitchburg

DEATHS

CLUTE — Howard M. Clute, M.D., of Boston, died September 19. He was in his fifty-seventh year.

Dr. Clute received his degree from Dartmouth Medical School in 1914. He was professor of surgery at Boston University School of Medicine and was a member of the New England Surgical Society, the American Surgical Association and the Southern Surgical Association and a fellow of the American College of Surgeons and the American Medical Association.

His widow, a son and a daughter survive.

MARSDEN — George Marsden, M.D., of New Bedford, died May 20. He was in his sixty-ninth year.

Dr. Marsden received his degree from Johns Hopkins University School of Medicine in 1906. He was a fellow of the American Medical Association.

O'BRIEN — Thomas F. O'Brien, M.D., of Worcester, died September 16. He was in his fifty-first year.

Dr. O'Brien received his degree from Harvard Medical School in 1921. He was a member of the New England Obstetrical and Gynecological Society and a fellow of the American College of Surgeons and the American Medical Association.

TINKHAM — Oliver G. Tinkham, M.D., of Newton, died September 10. He was in his sixty-seventh year.

Dr. Tinkham received his degree from Tufts College Medical School in 1905. He was a member of the New England Obstetrical and Gynecological Society and a fellow of the American College of Surgeons and the American Medical Association.

His widow and a son survive.

BOOK REVIEWS

Hayfever Plants: Their appearance, distribution and time of flowering, and their role in hayfever, with special reference to North America. By Roger P. Wodehouse, Ph.D. 4°, cloth, 245 pp., with 73 illustrations. A publication of the Chronica Botanica Company, Waltham, Massachusetts. New York City: G. E. Stechert and Company, 1945. $4.75.

This valuable monograph brings together for the first time in one volume all the plants whose pollens cause, or are suspected of causing, hay fever. The arrangement is botanical, following the sequence of Engler and Prantl. The plants described fall into two classes — the gymnosperms, which are relatively few, and the angiosperms, which comprise the majority. Botanical and common names are used in the descriptions, which are well written and sufficient for their purpose, including the physical characteristics, distribution, time of flowering and the part the plants play in the causation of hay fever. The numerous illustrations of flowers and pollens should prove useful for identification.

The work is divided into two main parts: the first discusses pollen and pollination and the role of pollen in hay fever; and the second consists of a series of regional surveys

covering areas in the United States, Canada and Mexico. The United States is divided into ten regions, and only the noxious plants are described for each region.

An interesting short chapter on the botany of hay fever, in which atmospheric pollen is considered, is found at the beginning of the book, and a selected bibliography is appended to the text.

The book is well printed with a good type on nonglare paper, with good margins.

This monograph is recommended for all physicians coming into contact with allergic disturbances, as well as for all medical, public and reference libraries.

Facial Prosthesis. By Arthur H. Bulbulian, M.S., D.D.S. 8°, cloth, 241 pp., with 202 illustrations. Philadelphia: W. B. Saunders Company, 1945. $5.00.

The reconstructive surgeon is constantly confronted with problems involving prosthetic restorations. The general surgeon in the treatment of cancer and major trauma also not infrequently has cases in which prosthetic restorations, either temporary or permanent, have much to offer. As the author plainly states, the repair of facial deformities is primarily a surgical problem, but there are numerous conditions and circumstances that make surgery impossible or inadvisable. In such a case a prosthetic device may be the answer. Prosthetic restorations of the missing parts of the extremities have long been an accepted orthopedic procedure, but surgery knows little about the possibility of prosthetic restoration of deformities of the face and jaws. One reason is that this specialty has been developed by dentists, and dental literature and subject matter are almost exclusively in dental periodicals and books. Secondly, since this is a highly specialized subject, few in the dental profession have taken the necessary training for the construction of such complicated prosthetic devices as are needed for facial and maxillary problems.

This concise book will undoubtedly fill a great demand, since at the present time there seems to be more interest in facial prosthesis than ever before. The author limits his subject, however, to the diagnosis of artificial restorations of the face, especially of the ears, nose and orbits; he does not consider maxillary restorations, which are often part of such deformities.

According to the opinion of the reviewer, the author has somewhat overemphasized the use of latex as a suitable material for restoration and has not given sufficient emphasis to other materials, such as acrylics.

The book is divided into fourteen chapters, and the classification of subjects is excellent. There are numerous diagrams and illustrations to help the reader in carrying out the technics of restoration. It is a good, small book to introduce prosthetic concepts and technics to the person interested in restorative problems of the face.

Pulmonary Tuberculosis in the Adult: Its fundamental aspects. By Max Pinner, M.D. 8°, cloth, 579 pp., with 59 illustrations and 3 graphs. Springfield, Illinois: Charles C Thomas, 1945. $7.50.

This book, written by a lifelong student of tuberculosis, is a treatise on clinical tuberculosis from the standpoint of the pathologist. In a protean disease like tuberculosis, with its multiple manifestations, a proper understanding of the physiopathology and its relation to immunity and allergy is of great practical importance. In the preface — the "apologia," as the author calls it — it is stated that the main purpose of the book is not to add another text on tuberculosis or to tell the practitioner how to do this or that, but to harmonize the clinical point of view with the broad aspects of pathological, bacteriologic and immunologic facts.

Out of nineteen chapters, only four can be classed as dealing with bedside observations and treatments. The other fifteen delve deeply into such subjects as histogenesis, immunologic and phthisiogenetic principles, typical lesions of pulmonary tuberculosis, with autoptic examples, and physiologic principles of respiration, to mention only a few of the topics. These chapters reflect the viewpoint of the author, who insisted for many years that an understanding of the basic principles of pathology is the key to intelligent treatment of tuberculosis — this is not to say that he completely neglects the clinical side. Diagnostic criteria are thoroughly discussed, and medical as well as collapse therapy is fully evaluated. The physiology of respiration and the physiologic and pathological correlations of collapse therapy receive due attention.

An added feature is the abstracted bibliography, in which the articles are briefly discussed and comments and criticisms added. This should be most helpful to the reader who can at a glance obtain all the divergent points of view written in the last two or three decades.

The text is written in an easy and clear style and is illustrated by well chosen and excellently reproduced microscopic as well as radiologic pictures. It is a book for the student or the specialist of tuberculosis. It is not intended for the undergraduate or general practitioner. This volume should find a place in the library of anyone interested in any of the many phases of pulmonary tuberculosis.

The Principal Nervous Pathways: Neurological charts and schemes with explanatory notes. By Andrew T. Rasmussen, Ph.D. Third edition. 4°, cloth, 73 pp. New York: The Macmillan Company, 1945.

This outstanding contribution to neuroanatomy, first published in 1932, has been revised at proper intervals. It is one of the best books on the subject and can be fully recommended. The author's position in the field is outstanding, and the book reflects his continued activity in presenting the most recent advances in neuroanatomy. In the new edition he has made definite modifications in some of the charts and minor alterations in others. When doubt exists, the author does not hesitate to query the finding, thus indicating the broad basis of his researches and always seeking a definitive point of view. The book is highly recommended.

Report of the National Health Survey. Conducted by Canadian Medical Procurement and Assignment Board. 8°, paper, 336 pp. Ottawa: Edmond Cloutier, 1945.

The primary function of the Canadian Medical Procurement and Assignment Board, established in July, 1932, was to obtain physicians for the armed forces and at the same time to provide adequate medical service for the civilian population. It became apparent that the health services of the country needed to be studied, and that this involved physicians, dentists, nurses, hospitals, medical schools, public health, medical research, industrial medicine, and the communities generally. This volume is a report of that study. Although much of the report pertains to the war period, parts of it will be of use in later years. It is doubtful whether this book will be of much interest to the average practitioner of medicine, but it will be valuable to the small group interested in such problems.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Bibliography of Infantile Paralysis, 1789-1944: With selected abstracts and annotations. Prepared under direction of the National Foundation for Infantile Paralysis, Inc. Edited by Morris Fishbein, M.D., editor, *Journal of the American Medical Association.* Compiled by Ludvig Hektoen, M.D., and Ella M. Salmonsen. 4°, cloth, 672 pp. Philadelphia: J. B. Lippincott Company, 1946.

This selective bibliography covers the clinical and investigative work on infantile paralysis appearing in monographs, pamphlets and theses since its description by Underwood in 1789. Little or no attention is paid to textbooks, systems of medicine, encyclopedias, the official publications of boards of health and pamphlets devoted to general health education, except when representing innovations. The scientific medical literature of the last few years from foreign countries is not complete, since the material has not been easily accessible. Future supplements are planned for the purpose of remedying this defect. The material is arranged chronologically, each reference is numbered, and there are two comprehensive indexes of authors and subjects. The volume is recommended as a reference text for all medical and public-health libraries.

A Primer of Electrocardiography. By George Burch, M.D., associate professor of medicine, Tulane University School of Medicine, senior visiting physician, Charity Hospital, consultant in cardiovascular diseases, Ochsner Clinic, and visiting physician, Touro Infirmary, New Orleans; and Travis Winsor, M.D., instructor in medicine, Tulane University School of Medicine, and assistant visiting physician, Charity Hospital, New Orleans. 8°, cloth, 215 pp., with 235 illustrations. Philadelphia: Lea and Febiger, 1945. $3.50.

This primer was written to enable the student who is unfamiliar with the subject to grasp a fundamental knowledge of electrocardiography in the most direct manner. Photographs of electrocardiograms have been excluded but diagrams are literally employed to illustrate typical electrocardiographic patterns. The material is presented from a mechanistic point of view as only with the knowledge of the mechanism is it possible for the reader of electrocardiograms to unravel individual tracings. The presentation has been kept simple and brief as the work is designed to supplement the many monographs on electrocardiography that are now available.

The Art of Medicine in Relation to the Progress of Thought: A lecture in the history of science course in the University of Cambridge February 10, 1945. By A. E. Clark-Kennedy, M.D., F.R.C.P., physician to the London Hospital and dean of the Medical School and fellow of Corpus Christi College, Cambridge. 12°, paper, 48 pp. Cambridge, England: University Press, 1945. 75 cents.

In this lecture Dr. Clark-Kennedy devotes most of his text to modern medicine in relation to current thought. To complete his task, however, he has made a brief review of the three periods of the past from Hippocrates to Descartes.

Clinical Traumatic Surgery. By John J. Moorhead, M.D., D.Sc., medical director, New York City Transit System, and consulting surgeon, Post-Graduate Hospital, United States Public Health Service, All Souls (Morristown), Anne May Memorial (Spring Lake), Caledonian, Harlem, Mary Immaculate (Jamaica), Mother Cabrini, New Rochelle, Nyack, Rockland State, St. Francis (Port Jervis) and Yonkers General hospitals. 8°, cloth, 747 pp., with 500 illustrations. Philadelphia: W. B. Saunders Company, 1945. $10.00.

This book has been written with the main idea of placing in one volume all the information necessary to diagnose the usual and most of the unusual effects of accident and injury. The author has summed up his two-score years of active experience in the field and has drawn on the subject matter of his teaching courses at postgraduate medical schools. The work is well printed on good paper but is rather heavy for its size.

Government in Public Health. By Harry S. Mustard, M.D., LL.D., DeLamar Professor of Public Health Practice, and director, School of Public Health, Faculty of Medicine, Columbia University. 8°, cloth, 219 pp., with 11 tables. New York: The Commonwealth Fund, 1945. $1.50.

Dr. Mustard in this monograph brings out the rapid extension of the field of public health as one of the important trends in modern medicine. He traces the development of state health departments and describes their proper sphere of action. The volume is issued as one of the series published under the auspices of the Committee on Medicine and the Changing Order of the New York Academy of Medicine.

One Hundred Years of Gynaecology, 1800–1900: A comprehensive review of the specialty during its greatest century, with summaries and case reports of all diseases pertaining to women. By James V. Ricci, M.D., clinical professor of gynecology and obstetrics, New York Medical College, director of gynecology of the City Hospital, New York, director of gynecology and obstetrics, Columbus Hospital, attending gynecologist and obstetrician, Flower and Fifth Avenue hospitals, New York, and consultant in gynecology and obstetrics, Downtown Hospital, New York. 4°, cloth, 651 pp. Philadelphia: The Blakiston Company, 1945. $8.50.

The author has attempted to survey the gynecologic literature of the nineteenth century and in conjunction with his previous volume, *The Genealogy of Gynaecology* (1943), provides a history of the subject from 2000 B.C. to 1900 A.D. This work should prove of value as a reference text and should be in all medical libraries.

NOTICES

ANNOUNCEMENTS

Dr. Charles Bushold, having returned from the armed services, is resuming practice at 351 Essex Street, Lawrence.

Dr. Henry M. Gahan announces his return from military service and resumption of practice at 19 Washington Street, Medford.

Dr. Louis Nathan, having returned from military service, is resuming practice at 276 Commonwealth Avenue, Boston.

EXHIBITION IN COMMEMORATION OF ETHER CENTENARY

The Boston Medical Library, in conjunction with the Boston Public Library and the Massachusetts Historical Society, will hold an exhibition in commemoration of the Ether Centenary, in the Treasure Room of the Boston Public Library, from October 15 to December 15.

The material exhibited will occupy all the cases in the Treasure Room and will cover the period from the beginnings of anesthesia, about 4000 B.C., to 1846. Emphasis will be placed on the work of Dr. William T. G. Morton.

AMERICAN ACADEMY OF ALLERGY

The American Academy of Allergy will hold its annual convention at the Hotel Pennsylvania, New York City, from November 25 to 27 inclusive. All physicians interested in allergic problems are cordially invited to attend the sessions as guests of the Academy without payment of registration fee. The program has been arranged to cover a wide variety of conditions in which allergic factors may be important. Papers will be presented dealing with the latest methods of diagnosis and treatment as well as the results of investigation and research. Advance copies of the program may be obtained by writing to Dr. Horace S. Baldwin, chairman on arrangements, 136 East 64th Street, New York City, prior to November 10.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

The first postwar meeting of the American Academy of Dermatology and Syphilology will be held at the Hotel Statler, Cleveland, Ohio, from December 7 to 12 inclusive, with daily symposiums at the Allerton Hotel and teaching clinics at the Cleveland City Hospital. Dr. Howard M. Cole, of Cleveland, will be in charge of local arrangements.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 17

FRIDAY, OCTOBER 18

*9:00–10:00 a.m. Recent Studies in Hemorrhagic Shock. Dr. Arnold M. Seligman. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical Staff Rounds, Peter Bent Brigham Hospital.

MONDAY, OCTOBER 21

*12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

(*Notices continued on page xvii*)